



Clinical trial results: A Phase II Study of PM01183 as Second-line Treatment in Patients with Metastatic Pancreatic Cancer.

Summary

EudraCT number	2010-024292-30
Trial protocol	GB ES
Global end of trial date	28 November 2013

Results information

Result version number	v1 (current)
This version publication date	29 July 2016
First version publication date	29 July 2016

Trial information

Trial identification

Sponsor protocol code	PM1183-B-001-10
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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-Norte, Colmenar Viejo, Madrid, Spain, 28770
Public contact	Clinical Development Department of PharmaMar's Oncology, Business Unit., Pharma Mar, S.A., +34 918466000, clinicaltrials@pharmamar.com
Scientific contact	Clinical Development Department of PharmaMar's Oncology, Business Unit., Pharma Mar, S.A., +34 918466000, 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	18 September 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 November 2013
Global end of trial reached?	Yes
Global end of trial date	28 November 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the antitumor activity of PM01183 in terms of overall survival rate at 6 months (OS6) in patients with metastatic pancreatic cancer.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and was consistent with the Good Clinical Practice (GCP) and applicable regulatory requirements. Study personnel involved in conducting this trial was qualified by education, training, and experience to perform their respective task(s).

The Sponsor provided insurance or indemnity in accordance with the applicable regulatory requirements.

Background therapy:

All patients had to receive standard prophylactic medication at least 30 minutes before the administration of PM01183, as follows:

- Corticosteroids (dexamethasone 8 mg i.v. or equivalent)
- Serotonin (5-HT3) antagonists (ondansetron 8 mg i.v. or equivalent)

Evidence for comparator: -

Actual start date of recruitment	29 June 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 33
Country: Number of subjects enrolled	United Kingdom: 12
Worldwide total number of subjects	45
EEA total number of subjects	45

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)	26
From 65 to 84 years	19
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 45 patients were enrolled at seven investigational sites, and 44 of them were treated with PM01183. The patients participated in this study between 29 June 2011 (first consent) and 28 November 2013 (last follow-up). First and last infusions were administered on 11 July 2011 and 3 July 2013, respectively

Pre-assignment

Screening details:

Voluntary written IC, 18-75 years, Histologically/cytologically confirmed cancer of the exocrine pancreas, Stage IV disease, Patient had to have progressed during or after one prior line of gemcitabine based therapy, ECOG PS \leq 1, Adequate hematological, renal, metabolic and hepatic function, At least two weeks since last prior therapy

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	PM01183
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Arm description:

PM01183 was given at a dose of 7.0 mg FD as a 1-hour q3wk i.v. infusion. Each cycle lasted three weeks.

Arm type	Experimental
Investigational medicinal product name	PM01183
Investigational medicinal product code	PM01183
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

PM01183 was given at a dose of 7.0 mg FD as a 1-hour q3wk i.v. infusion. Each cycle lasted three weeks

Number of subjects in period 1	PM01183
Started	45
Treated	44
Completed	0
Not completed	45
Adverse event, serious fatal	3
Clinical progression	2
Consent withdrawn by subject	1
Physician decision	1
Adverse event, non-fatal	1

Clinical deterioration	1
Death due to malignant disease	5
Progressive disease	30
Not treated	1

Baseline characteristics

Reporting groups

Reporting group title	Overall period
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Reporting group description: -

Reporting group values	Overall period	Total	
Number of subjects	45	45	
Age categorical			
Units: Subjects			
18-49 years	2	2	
50-69 years	36	36	
>=70 years	7	7	
Age continuous			
Units: years			
median	62		
full range (min-max)	42 to 83	-	
Gender categorical			
Units: Subjects			
Female	32	32	
Male	13	13	
Race			
Units: Subjects			
Caucasian	42	42	
Black	1	1	
Arabic	2	2	
ECOG			
Eastern Cooperative Oncology Group performance status			
Units: Subjects			
PS 0	8	8	
PS 1	37	37	
Elevated CA19-9			
Units: Subjects			
Yes	41	41	
No	4	4	
Pain control medication			
Units: Subjects			
Fully controlled	9	9	
Controlled most of the time	19	19	
Controlled < 50% of time	3	3	
No	14	14	
Opioid consumption			
Units: Subjects			
Yes	16	16	
No	29	29	
Primary tumor location (pancreas)			
Units: Subjects			
Head	28	28	

Body/tail	16	16	
Head + body/tail	1	1	
Tumor stage at diagnosis Units: Subjects			
Metastatic	23	23	
Locally advanced	17	17	
Early	5	5	
Histology grade Units: Subjects			
Well differentiated	4	4	
Moderately differentiated	11	11	
Poorly differentiated	7	7	
UK	23	23	
Current disease (metastatic) Units: Subjects			
Visceral	19	19	
Ganglionar/Peritoneal	8	8	
Both	18	18	
No. of sites of disease Units: Subjects			
1 site	10	10	
2 sites	19	19	
3 sites	10	10	
4 sites	5	5	
8 sites	1	1	
Chemoradiotherapy Units: Subjects			
Yes	7	7	
No	38	38	
Surgery Units: Subjects			
Yes	24	24	
No	21	21	
Setting of Chemotherapy Units: Subjects			
Advanced	34	34	
Adjuvant	9	9	
Adjuvant+advanced	2	2	
Most frequent prior chemotherapy regimens Units: Subjects			
Gemcitabine	15	15	
Gemcitabine + capecitabine	8	8	
Gemcitabine + oxaliplatin	8	8	
Gemcitabine + paclitaxel	4	4	
Gemcitabine + 5-FU	3	3	
Gemcitabine + Others	7	7	
Best response to last prior chemotherapy Units: Subjects			
PR	4	4	
SD	15	15	

PD	10	10	
NA	5	5	
UK	11	11	
Signs and symptoms			
Units: Subjects			
0 sign/symptom	8	8	
1 sign/symptom	16	16	
2 signs/symptoms	10	10	
3 signs/symptoms	6	6	
4 signs/symptoms	4	4	
5 signs/symptoms	1	1	
Physical examination			
Units: Subjects			
Normal	41	41	
Abnormal	4	4	
ECG			
Electrocardiogram			
Units: Subjects			
Normal	32	32	
Abnormal	13	13	
LVEF			
left ventricular ejection fraction			
Units: Subjects			
Normal	44	44	
Abnormal	1	1	
BSA			
body surface area			
Units: m2			
median	1.76		
full range (min-max)	1.29 to 2.44	-	
Albumin			
Units: g/dl			
median	3.9		
full range (min-max)	2.6 to 4.9	-	
CA19-9			
Units: IU/l			
median	1965		
full range (min-max)	0.6 to 153230	-	
Time from diagnosis to first PM01183 infusion			
Units: months			
median	7.3		
full range (min-max)	2.5 to 34.8	-	
Time from last disease progression before study entry to first PM01183 infusion			
Units: months			
median	0.7		
full range (min-max)	0.1 to 11.1	-	
No. of sites of disease			
Units: sites			
median	2		

full range (min-max)	1 to 8	-	
No. of agents of Chemotherapy Units: No. of agents median full range (min-max)	2 1 to 3	-	
TTP to last prior advanced chemotherapy Units: months median full range (min-max)	4.6 1.4 to 23.4	-	
Signs and symptoms Units: signs and symptoms median full range (min-max)	1 0 to 5	-	
Weight Units: kilogram(s) median full range (min-max)	68.7 38.5 to 113.5	-	
Height Units: cm median full range (min-max)	168 151 to 193	-	
BMI			
body mass index			
Units: kg/m2 median full range (min-max)	24.1 16.9 to 36.8	-	
WBC Units: x10 ⁹ /l median full range (min-max)	6.8 3.3 to 15.7	-	
Hemoglobin Units: g/dl median full range (min-max)	12.1 9.5 to 14.9	-	
Platelets Units: x10 ⁹ /l median full range (min-max)	248 110 to 571	-	
Neutrophils Units: x10 ⁹ /l median full range (min-max)	4.1 1.7 to 12.2	-	
Lymphocytes Units: x10 ⁹ /l median full range (min-max)	1.5 0.6 to 4	-	
ALT Units: xULN median full range (min-max)	0.6 0.2 to 2.8	-	
AP			

Units: xULN median full range (min-max)	1.2 0.4 to 3.8	-	
AST Units: xULN median full range (min-max)	0.7 0.4 to 3.7	-	
CPK Units: xULN median full range (min-max)	0.3 0.1 to 1.9	-	
Creatinine Units: xULN median full range (min-max)	0.6 0.4 to 1	-	
GGT Units: xULN median full range (min-max)	1.4 0.3 to 21.6	-	
Total bilirubin Units: xULN median full range (min-max)	0.5 0.2 to 1.7	-	
Calcium Units: mmol/l median full range (min-max)	2.3 2.1 to 2.7	-	
Potassium Units: mmol/l median full range (min-max)	4.2 3.6 to 5.3	-	
Sodium Units: mmol/l median full range (min-max)	139 127 to 144.5	-	
Total cholesterol Units: mg/dl median full range (min-max)	177.9 85 to 249	-	

End points

End points reporting groups

Reporting group title	PM01183
Reporting group description: PM01183 was given at a dose of 7.0 mg FD as a 1-hour q3wk i.v. infusion. Each cycle lasted three weeks.	

Primary: Overall Survival Rate at Six Months

End point title	Overall Survival Rate at Six Months ^[1]
End point description:	
End point type	Primary
End point timeframe: Six months after the first PM01183 dose of each patient	

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: Primary endpoint (OS6) to test the null hypothesis that 25% or less patients were alive six months after the first infusion

End point values	PM01183			
Subject group type	Reporting group			
Number of subjects analysed	43 ^[2]			
Units: Subjects				
Yes	14			
No	29			

Notes:

[2] - OS6 was thus 32.6% (95% CI: 19.1-48.5%)

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Response Rate

End point title	Overall Response Rate
End point description: NE, not evaluable; PD, progressive disease; PR, partial response; SD, stable disease	
Response rate (95% CI) (patients evaluable for efficacy, n=43) 2.3% (0.1-12.3%) Response rate (95% CI) (patients evaluable for response, n=42) 2.4% (0.1-12.6%) (One patient died due to toxicity before the first tumor evaluation and was excluded from the population of patients evaluable for response)	
End point type	Secondary
End point timeframe: Overall period	

End point values	PM01183			
Subject group type	Reporting group			
Number of subjects analysed	43			
Units: Subjects				
PR	1			
SD	15			
PD	26			
NE	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free Survival

End point title	Progression-free Survival
End point description:	
End point type	Secondary
End point timeframe:	
Overall period	

End point values	PM01183			
Subject group type	Reporting group			
Number of subjects analysed	43 ^[3]			
Units: months				
median (confidence interval 95%)	1.4 (1.2 to 2.3)			

Notes:

[3] - Events (%) 40 (93.0%)

Attachments (see zip file)	Kaplan-Meier plot of progression-free survival.bmp
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Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free survival Rates

End point title	Progression-free survival Rates
End point description:	
End point type	Secondary
End point timeframe:	
at Three and Six Months after the first PM01183 dose	

End point values	PM01183			
Subject group type	Reporting group			
Number of subjects analysed	43			
Units: percentage				
arithmetic mean (confidence interval 95%)				
PFS3	27.5 (14.1 to 41)			
PFS6	14.6 (3.6 to 25.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

End point title	Overall Survival
End point description:	
End point type	Secondary
End point timeframe:	
Overall period	

End point values	PM01183			
Subject group type	Reporting group			
Number of subjects analysed	43 ^[4]			
Units: months				
arithmetic mean (confidence interval 95%)	4 (3.1 to 5.4)			

Notes:

[4] - Events (%): 41 (95.3%)

Attachments (see zip file)	Kaplan-Meier plot of overall survival.bmp
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Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival Rate

End point title	Overall Survival Rate
End point description:	

End point type	Secondary
End point timeframe: at 12 Months after the first PM01183 dose	

End point values	PM01183			
Subject group type	Reporting group			
Number of subjects analysed	43			
Units: percentage				
arithmetic mean (confidence interval 95%)	9.3 (0.6 to 18)			

Statistical analyses

No statistical analyses for this end point

Secondary: Evolution of Tumor Marker CA19-9

End point title	Evolution of Tumor Marker CA19-9
End point description:	

End point type	Secondary
End point timeframe: During Treatment	

End point values	PM01183			
Subject group type	Reporting group			
Number of subjects analysed	35 ^[5]			
Units: Subjects				
Decrease	14			
No decrease	21			

Notes:

[5] - High CA19-9 levels at baseline

Attachments (see zip file)	CA19-9 variation.bmp
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Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic parameters (CL)

End point title	Pharmacokinetic parameters (CL)
End point description:	

End point type	Secondary
End point timeframe:	
Treatment	

End point values	PM01183			
Subject group type	Reporting group			
Number of subjects analysed	44 ^[6]			
Units: l/h				
median (standard deviation)				
Cycle 1	12.5 (± 7)			
Cycle 2	13.4 (± 8.2)			

Notes:

[6] - Cycle 1: N=44

Cycle 2: N=33

Attachments (see zip file)	Total body clearance per cycle.bmp
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Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Overall period

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	11.0
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Reporting groups

Reporting group title	PM01183
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Reporting group description:

PM01183 was given at a dose of 7.0 mg FD as a 1-hour q3wk i.v. infusion. Each cycle lasted three weeks.

Serious adverse events	PM01183		
Total subjects affected by serious adverse events			
subjects affected / exposed	32 / 44 (72.73%)		
number of deaths (all causes)	42		
number of deaths resulting from adverse events	3		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Blood bilirubin increased			
subjects affected / exposed	2 / 44 (4.55%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Blood creatine increased			
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Neoplasms benign, malignant and unspecified (incl cysts and polyps) tumour associated fever subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 44 (2.27%) 0 / 1 0 / 0		
tumour pain subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 44 (2.27%) 0 / 1 0 / 0		
Vascular disorders Hypertensive crisis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 44 (2.27%) 0 / 1 0 / 0		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	5 / 44 (11.36%) 5 / 6 0 / 0		
Febrile neutropenia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	9 / 44 (20.45%) 11 / 11 0 / 0		
Neutropenia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	5 / 44 (11.36%) 6 / 6 1 / 1		
Thrombocytopenia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	11 / 44 (25.00%) 16 / 16 0 / 0		
General disorders and administration site conditions Fatigue			

subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 44 (4.55%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Intestinal obstruction			
subjects affected / exposed	2 / 44 (4.55%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Nausea			
subjects affected / exposed	2 / 44 (4.55%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Rectal haemorrhage			
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	5 / 44 (11.36%)		
occurrences causally related to treatment / all	2 / 5		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	2 / 44 (4.55%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
haemoptysis			
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		

Pneumonitis			
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumothorax			
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	2 / 44 (4.55%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute prerenal failure			
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haematuria			
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Renal failure			
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Renal failure acute			
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bacteraemia			
subjects affected / exposed	1 / 44 (2.27%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Bronchopneumopathy				
subjects affected / exposed	1 / 44 (2.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Escherichia infection				
subjects affected / exposed	1 / 44 (2.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Escherichia sepsis				
subjects affected / exposed	1 / 44 (2.27%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Klebsiella bacteraemia				
subjects affected / exposed	1 / 44 (2.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Liver abscess				
subjects affected / exposed	1 / 44 (2.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Neutropenic sepsis				
subjects affected / exposed	1 / 44 (2.27%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			
Pneumonia				
subjects affected / exposed	1 / 44 (2.27%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	1 / 44 (2.27%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Septic shock				

subjects affected / exposed	2 / 44 (4.55%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 44 (2.27%)		
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	PM01183		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	44 / 44 (100.00%)		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	3 / 44 (6.82%)		
occurrences (all)	3		
Weight decreased			
subjects affected / exposed	8 / 44 (18.18%)		
occurrences (all)	12		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	23 / 44 (52.27%)		
occurrences (all)	73		
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 44 (6.82%)		
occurrences (all)	3		
Phlebitis			
subjects affected / exposed	3 / 44 (6.82%)		
occurrences (all)	6		
Cardiac disorders			
Tachycardia			
subjects affected / exposed	4 / 44 (9.09%)		
occurrences (all)	17		

Nervous system disorders Lethargy subjects affected / exposed occurrences (all)	3 / 44 (6.82%) 9		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) Neutropenia subjects affected / exposed occurrences (all) Thrombocytopenia subjects affected / exposed occurrences (all)	8 / 44 (18.18%) 14 12 / 44 (27.27%) 16 5 / 44 (11.36%) 5		
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) Oedema peripheral subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all)	28 / 44 (63.64%) 118 7 / 44 (15.91%) 13 12 / 44 (27.27%) 14		
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) Ascites subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Diarrhoea	9 / 44 (20.45%) 19 3 / 44 (6.82%) 3 13 / 44 (29.55%) 20		

<p>subjects affected / exposed occurrences (all)</p> <p>Nausea subjects affected / exposed occurrences (all)</p> <p>Vomiting subjects affected / exposed occurrences (all)</p>	<p>14 / 44 (31.82%) 40</p> <p>28 / 44 (63.64%) 58</p> <p>20 / 44 (45.45%) 42</p>		
<p>Respiratory, thoracic and mediastinal disorders</p> <p>Cough subjects affected / exposed occurrences (all)</p> <p>Dyspnoea subjects affected / exposed occurrences (all)</p> <p>Hiccups subjects affected / exposed occurrences (all)</p>	<p>3 / 44 (6.82%) 4</p> <p>7 / 44 (15.91%) 8</p> <p>4 / 44 (9.09%) 6</p>		
<p>Psychiatric disorders</p> <p>Depression subjects affected / exposed occurrences (all)</p>	<p>4 / 44 (9.09%) 10</p>		
<p>Musculoskeletal and connective tissue disorders</p> <p>Back pain subjects affected / exposed occurrences (all)</p>	<p>3 / 44 (6.82%) 6</p>		
<p>Metabolism and nutrition disorders</p> <p>Decreased appetite subjects affected / exposed occurrences (all)</p>	<p>16 / 44 (36.36%) 29</p>		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 January 2011	This protocol amendment included the following changes: 1. Included the collection of an additional blood sample from patients who consented to the PGx substudy, immediately before treatment with PM01183, to perform a gene expression profile (GEP) on purified circulating tumor cell (CTC)-enriched fractions. 2. Added contact information for the Central Laboratory for PGx Analyses.
21 November 2011	Included the following changes 1. Updated contact information for the Sponsor 2. Clarified: the protocol sections describing the laboratories for PGx tissue and blood sample processing and analysis and the inclusion criteria to allow the recruitment of patients who failed gemcitabine-containing adjuvant therapy within six months and with metastatic disease at study entry 3. Changed the inclusion criteria to set a maximum accepted age of 75 years-old, the inclusion criterion regarding bilirubin levels to require patients to have both total bilirubin $\leq 1.5 \times \text{ULN}$ and direct bilirubin $\leq \text{ULN}$ and the inclusion criterion regarding albumin levels 4. Clarified the eligibility criteria to exclude patients with rapidly deteriorating pancreatic cancer and/or uncontrolled symptoms, and patients who require or carry external drainage catheters (which are associated with an increased risk of infection) 5. Updated the inclusion criteria to reflect that the period of time that female patients must avoid becoming pregnant after treatment discontinuation had decreased from six months to six weeks, following the finding that only untraceable levels of PM01183 remain after six weeks 6. Updated information on the authorized formulations of PM01183 7. Updated the hemoglobin value allowed for treatment continuation to make it consistent with the inclusion criteria 8. Increased the albumin value allowed for treatment continuation, due to the relevance of albumin levels as an independent prognostic factor in pancreatic cancer 9. Clarified the rules for replacing patients and for considering patients evaluable for efficacy 10. Changed the collection time of a blood sample for PGx analysis to "any time before the start of the second PM01183 infusion", as extending the collection period would help study logistics and treatment planning 11. Removed the description of the handling of PK samples in the protocol

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported