



## Clinical trial results:

### A Phase II Study of Nab-paclitaxel and Gemcitabine, in Elderly Patients with Previously Untreated, Metastatic Pancreatic Adenocarcinoma

#### Summary

EudraCT number	2014-003596-27
Trial protocol	ES
Global end of trial date	15 March 2019

#### Results information

Result version number	v1 (current)
This version publication date	11 August 2021
First version publication date	11 August 2021

#### Trial information

##### Trial identification

Sponsor protocol code	BIBABRAX
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##### Additional study identifiers

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

Notes:

#### Sponsors

Sponsor organisation name	ASONMEC (Asociación de Oncología Médica del Hospital de Cruces)
Sponsor organisation address	Plaza de Cruces, s/n, Baracaldo, Vizcaya, Spain, 48903
Public contact	Departamento Operaciones Clínicas, APICES SOLUCIONES, S.L., +34 918166804103, ana.moreno@apices.es
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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	15 April 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 March 2019
Global end of trial reached?	Yes
Global end of trial date	15 March 2019
Was the trial ended prematurely?	No

Notes:

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**General information about the trial**

Main objective of the trial:

To evaluate the efficacy of treatment through 3-months deterioration free rate

Protection of trial subjects:

Not applicable.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 August 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

Country: Number of subjects enrolled	Spain: 80
Worldwide total number of subjects	80
EEA total number of subjects	80

Notes:

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**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)	0
From 65 to 84 years	78
85 years and over	2

## Subject disposition

### Recruitment

Recruitment details:

Patients were included in the study between 5th August 2015 and 6th September 2017.

### Pre-assignment

Screening details:

98 patients were recruited initially in the study which were analyzed 80. 18 patients were screening failures.

### Period 1

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

### Arms

<b>Arm title</b>	Study treatment
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Arm description:

Patients received nab-paclitaxel 125 mg/m<sup>2</sup> plus gemcitabine 1000 mg/m<sup>2</sup> at days 1, 8 and 15 of each cycle with 1 week off.

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

Dosage and administration details:

125 mg/m<sup>2</sup> at days 1, 8 and 15 of each cycle.

Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1000 mg/m<sup>2</sup> at days 1, 8 and 15 of each cycle.

Number of subjects in period 1	Study treatment
Started	80
Completed	51
Not completed	29
Physician decision	14
Adverse event, non-fatal	15



## Baseline characteristics

### Reporting groups

Reporting group title	Overall trial
Reporting group description: -	

Reporting group values	Overall trial	Total	
Number of subjects	80	80	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	78	78	
85 years and over	2	2	
Age continuous			
one patient indicated date of birth the date of informed consent.			
Units: years			
median	74.6		
full range (min-max)	70.0 to 87.9	-	
Gender categorical			
Units: Subjects			
Female	34	34	
Male	46	46	
ECOG-PS			
Units: Subjects			
(0)	23	23	
(1)	57	57	
Disease diagnosis			
Units: Subjects			
Pancreatic adenocarcinoma	70	70	
Ductal adenocarcinoma	6	6	
Pancreatic acinar carcinoma	1	1	
Pancreatobiliary adenocarcinoma	1	1	
Infiltrative adenocarcinoma	1	1	
Signet ring cell adenocarcinoma	1	1	
Current M status			
Units: Subjects			
M0	11	11	
M1	69	69	
Previous surgery			
Units: Subjects			
Yes	13	13	

No	67	67	
Previous chemotherapy			
One patient received 3 previous lines of gemcitabine in monotherapy, each completed on 1st July 2008, 21st December 2012 and 11th June 2013			
Units: Subjects			
Gemcitabine	9	9	
5-FU/LV	1	1	
5-FU	1	1	
No	69	69	
Previous radiotherapy			
Units: Subjects			
Yes	3	3	
No	77	77	
Number of patients per location: Pancreas			
Units: Subjects			
Yes	70	70	
No	10	10	
Number of patients per location: Liver			
Units: Subjects			
Yes	40	40	
No	40	40	
Number of patients per location: Lymph nodes			
Units: Subjects			
Yes	21	21	
No	59	59	
Number of patients per location: Lung			
Units: Subjects			
Yes	19	19	
No	61	61	
Number of patients per location: Peritoneum			
Units: Subjects			
Yes	16	16	
No	64	64	
Number of location per patient			
Units: Subjects			
(1)	17	17	
(2)	35	35	
>3	28	28	
Pancreatic tumor location: Head			
Units: Subjects			
Yes	26	26	
No	54	54	
Pancreatic tumor location: Tail			
Units: Subjects			
Yes	20	20	
No	60	60	
Pancreatic tumor location: Body			
Units: Subjects			
Yes	18	18	

No	62	62	
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Weight Units: Kg median full range (min-max)	67.0 41.9 to 88.0	-	
Height Units: Cm median full range (min-max)	161.5 142.0 to 178.0	-	
Body surface area Units: m2 median full range (min-max)	1.7 1.3 to 2.0	-	
Time since initial diagnosis Units: Months median full range (min-max)	0.9 0.0 to 108.5	-	
Number of cycles administered Units: Number of cycles median full range (min-max)	4.0 1.0 to 19.0	-	
Relative dose intensity of Nab-paclitaxel Units: (%) median full range (min-max)	74 32 to 100	-	
Relative dose intensity of Gemcitabine Units: (%) median full range (min-max)	76 32 to 110	-	

## End points

### End points reporting groups

Reporting group title	Study treatment
Reporting group description: Patients received nab-paclitaxel 125 mg/m <sup>2</sup> plus gemcitabine 1000 mg/m <sup>2</sup> at days 1, 8 and 15 of each cycle with 1 week off.	

### Primary: 3-months deterioration free rate

End point title	3-months deterioration free rate <sup>[1]</sup>
End point description: Deterioration free rate was defined as the time elapsed in months since patients entry into the study until clinical deterioration defined as a decrease of at least 10 points on the global health status score of the EORTC-QLQ-C-30 scale.	
End point type	Primary
End point timeframe: Every 4 weeks.	

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: Single-arm clinical trial. Only descriptive analyses performed. No comparisons.

End point values	Study treatment			
Subject group type	Reporting group			
Number of subjects analysed	80			
Units: (%)				
median (full range (min-max))				
3-months deterioration free rate	54.3 (41.6 to 67.0)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: 3 months progression free survival

End point title	3 months progression free survival
End point description: Progression free survival was defined as the time from the date of treatment to the first of either disease progression, relapse or death from any cause.	
End point type	Secondary
End point timeframe: 3 months	



End point values	Study treatment			
Subject group type	Reporting group			
Number of subjects analysed	80			
Units: (%)				
median (confidence interval 95%)	77.1 (67.7 to 86.5)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Time to tumor progression

End point title	Time to tumor progression
End point description:	
Time to tumor progression was defined as the time elapsed, in months, since date of treatment to the first of either disease progression.	
End point type	Secondary
End point timeframe:	
Every 4 weeks	

End point values	Study treatment			
Subject group type	Reporting group			
Number of subjects analysed	80			
Units: Months				
median (confidence interval 95%)				
Time to tumor progression	8.299 (6.327 to 10.252)			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Objective response

End point title	Objective response
End point description:	
Best treatment response.	
End point type	Secondary
End point timeframe:	
Every 8 weeks	

End point values	Study treatment			
Subject group type	Reporting group			
Number of subjects analysed	80			
Units: Percentage (%)				
number (confidence interval 95%)				
Objective response rate (CR + PR)	13.8 (6.2 to 21.3)			
Clinical Benefit Rate (CR + PR + EE)	67.5 (57.2 to 77.8)			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Overall Survival

End point title	Overall Survival
End point description:	
Overall survival has been defined as the time elapsed in months from patient entry into the study until death from any cause.	
End point type	Secondary
End point timeframe:	
Every 8 weeks	

End point values	Study treatment			
Subject group type	Reporting group			
Number of subjects analysed	79 <sup>[2]</sup>			
Units: Months				
median (confidence interval 95%)				
Overall Survival	9.211 (6.946 to 11.475)			

Notes:

[2] - One patient has not date of éxitus.

## 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) was defined as the time from the date of treatment to the first of either disease progression, relapse or death from any cause.	
End point type	Secondary
End point timeframe:	
Until disease progression.	

End point values	Study treatment			
Subject group type	Reporting group			
Number of subjects analysed	80			
Units: Months				
median (confidence interval 95%)				
Time of follow up (months)	7.171 (5.809 to 8.533)			

## Statistical analyses

No statistical analyses for this end point

### Secondary: CA 19-9 biomarker response

End point title	CA 19-9 biomarker response
End point description: CA 19-9 biomarker response has been defined as a reduction of at least 50% from baseline.	
End point type	Secondary
End point timeframe: Every 4 weeks	

End point values	Study treatment			
Subject group type	Reporting group			
Number of subjects analysed	71 <sup>[3]</sup>			
Units: Subjects				
Responder	25			
No responder	46			

Notes:

[3] - 9 patients do not indicate evaluation of CA 19-9 after baseline.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Toxicities grade 3-4 frequency higher than 10%

End point title	Toxicities grade 3-4 frequency higher than 10%
End point description: Number of subjects with asthenia grade 3-4: 17 Number of subjects with neurotoxicity grade 3-4: 13 Number of subjects with Neutropenia grade 3-4: 17 Number of total subjects with toxicities grade 3-4: 29	
End point type	Secondary

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End point timeframe:

Every 4 weeks.

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<b>End point values</b>	Study treatment			
Subject group type	Reporting group			
Number of subjects analysed	80			
Units: Percentage (%)				
number (not applicable)				
Asthenia	21.25			
Neurotoxicity	16.25			
Neutropenia	21.25			
Total	36.25			

### **Statistical analyses**

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Every 4 weeks.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	22.1
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### Reporting groups

Reporting group title	Overall Trial
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Reporting group description: -

Serious adverse events	Overall Trial		
Total subjects affected by serious adverse events			
subjects affected / exposed	68 / 80 (85.00%)		
number of deaths (all causes)	19		
number of deaths resulting from adverse events	9		
Vascular disorders			
Thrombosis venous deep			
subjects affected / exposed	3 / 80 (3.75%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Venous thrombosis deep (limbs)			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Clinical deterioration			
subjects affected / exposed	2 / 80 (2.50%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
Fever			
subjects affected / exposed	4 / 80 (5.00%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		

General physical health deterioration subjects affected / exposed	1 / 80 (1.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Asthenia subjects affected / exposed	1 / 80 (1.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Multiorgan failure subjects affected / exposed	2 / 80 (2.50%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		
Oedema lower limb subjects affected / exposed	1 / 80 (1.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Abdominal pain subjects affected / exposed	1 / 80 (1.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Worsening PS subjects affected / exposed	1 / 80 (1.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Respiratory, thoracic and mediastinal disorders			
Pulmonary thromboembolism subjects affected / exposed	1 / 80 (1.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dyspnoea subjects affected / exposed	3 / 80 (3.75%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		

Investigations			
Hypertransaminasaemia	Additional description: Hypertransaminasaemia related with gemcitabine and nab-paclitaxel.		
subjects affected / exposed	1 / 80 (1.25%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Pertrochanteric fracture of the femur, open			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Right frontal subacute stroke			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ischaemic stroke			
subjects affected / exposed	1 / 80 (1.25%)		
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 / 80 (1.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neutropenia	Additional description: 2 Neutropenias related with gemcitabine and nab-paclitaxel.		
subjects affected / exposed	2 / 80 (2.50%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Pancytopenia	Additional description: Pancytopenia related with gemcitabine.		

subjects affected / exposed	1 / 80 (1.25%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Leukopenia	Additional description: Leukopenia related with gemcitabine and nab-paclitaxel.		
subjects affected / exposed	1 / 80 (1.25%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Constipation	Additional description: Constipation related with Nab-paclitaxel.		
subjects affected / exposed	1 / 80 (1.25%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Intestinal obstruction			
subjects affected / exposed	3 / 80 (3.75%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Intestinal perforation	Additional description: Intestinal perforation related with gemcitabine and nab-paclitaxel.		
subjects affected / exposed	1 / 80 (1.25%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Diarrhoea	Additional description: 3 diarrhoea related with gemcitabine and nab-paclitaxel.		
subjects affected / exposed	4 / 80 (5.00%)		
occurrences causally related to treatment / all	3 / 5		
deaths causally related to treatment / all	0 / 0		
Colonic obstruction			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Paralysis ileum			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haemorrhage of digestive tract			



subjects affected / exposed	1 / 80 (1.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Hepatobiliary disorders			
Hepatotoxicity	Additional description: Hepatotoxicity related with gemcitabine.		
subjects affected / exposed	1 / 80 (1.25%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Obstructive jaundice			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Biliary vesicle perforation			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Jaundice			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pollakiuria			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
insufficiency renal			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue			

disorders			
Knee pain			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Escherechia coli bacteraemia			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory tract infection			
subjects affected / exposed	3 / 80 (3.75%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
Pneumonia			
subjects affected / exposed	3 / 80 (3.75%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Aeromona nyrrophylla and klebsiella pneumoniae bacteraemia	Additional description: Aeromona nyrrophylla and klebsiella pneumoniae bacteraemia related with gemcitabine and nab-paclitaxel.		
subjects affected / exposed	1 / 80 (1.25%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Herpes oesophagitis	Additional description: Herpes oesophagitis related with Gemcitabine and nab-paclitaxel.		
subjects affected / exposed	1 / 80 (1.25%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Reservoir infection			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Thrombophlebitis septic			

subjects affected / exposed	1 / 80 (1.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Multilobar pneumonia			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Skin infection			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary sepsis			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	1 / 80 (1.25%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diabetes mellitus inadequate control			
subjects affected / exposed	1 / 80 (1.25%)		
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 %

<b>Non-serious adverse events</b>	Overall Trial		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	80 / 80 (100.00%)		
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	4 / 80 (5.00%)		
occurrences (all)	4		
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	9 / 80 (11.25%)		
occurrences (all)	9		
Dizziness			
subjects affected / exposed	7 / 80 (8.75%)		
occurrences (all)	7		
Neuropathy peripheral			
subjects affected / exposed	19 / 80 (23.75%)		
occurrences (all)	19		
Neurotoxicity			
subjects affected / exposed	20 / 80 (25.00%)		
occurrences (all)	20		
Paraesthesia			
subjects affected / exposed	12 / 80 (15.00%)		
occurrences (all)	12		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	27 / 80 (33.75%)		
occurrences (all)	27		
Leukopenia			
subjects affected / exposed	6 / 80 (7.50%)		
occurrences (all)	6		
Neutropenia			
subjects affected / exposed	27 / 80 (33.75%)		
occurrences (all)	27		
Thrombocytopenia			
subjects affected / exposed	24 / 80 (30.00%)		
occurrences (all)	24		
General disorders and administration			

site conditions			
Asthenia			
subjects affected / exposed	65 / 80 (81.25%)		
occurrences (all)	65		
Peripheral oedema			
subjects affected / exposed	20 / 80 (25.00%)		
occurrences (all)	20		
Mucosal inflammation			
subjects affected / exposed	14 / 80 (17.50%)		
occurrences (all)	14		
Pyrexia			
subjects affected / exposed	17 / 80 (21.25%)		
occurrences (all)	17		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	33 / 80 (41.25%)		
occurrences (all)	33		
Dyspepsia			
subjects affected / exposed	5 / 80 (6.25%)		
occurrences (all)	5		
Abdominal pain			
subjects affected / exposed	25 / 80 (31.25%)		
occurrences (all)	25		
Abdominal pain upper			
subjects affected / exposed	6 / 80 (7.50%)		
occurrences (all)	6		
Constipation			
subjects affected / exposed	23 / 80 (28.75%)		
occurrences (all)	23		
Nausea			
subjects affected / exposed	21 / 80 (26.25%)		
occurrences (all)	21		
Vomiting			
subjects affected / exposed	12 / 80 (15.00%)		
occurrences (all)	12		
Respiratory, thoracic and mediastinal disorders			

Catarrh subjects affected / exposed occurrences (all)	4 / 80 (5.00%) 4		
Dyspnoea subjects affected / exposed occurrences (all)	11 / 80 (13.75%) 11		
Epistaxis subjects affected / exposed occurrences (all)	5 / 80 (6.25%) 5		
Cough subjects affected / exposed occurrences (all)	4 / 80 (5.00%) 4		
Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all)	24 / 80 (30.00%) 24		
Eruption subjects affected / exposed occurrences (all)	6 / 80 (7.50%) 6		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	6 / 80 (7.50%) 6		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	7 / 80 (8.75%) 7		
Back pain subjects affected / exposed occurrences (all)	5 / 80 (6.25%) 5		
Pain in extremity subjects affected / exposed occurrences (all)	5 / 80 (6.25%) 5		
Myalgia subjects affected / exposed occurrences (all)	6 / 80 (7.50%) 6		

Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	32 / 80 (40.00%) 32		
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## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 August 2015	Amendment 1: Protocol version 2.0

Notes:

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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.

Open-label single-arm study. No control group for comparison.

Notes: