Clinical trial results:
Randomized Phase II Study of Cabazitaxel Versus Topotecan in Small Cell Lung Cancer Patients With Progressive Disease During or After a First Line Platinum Based Chemotherapy

Summary

EudraCT number	2011-003415-31
Trial protocol	HU FR GR NO IT DE PL ES
Global end of trial date	02 April 2014

Results information

Result version number	v1 (current)
This version publication date	27 April 2016
First version publication date	15 July 2015

Trial information

Trial identification

Sponsor protocol code	ARD12166

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01500720
WHO universal trial number (UTN)	U1111-1123-3503

Notes:

Sponsors

Sponsor organisation name	Sanofi aventis recherche & développement
Sponsor organisation address	1 avenue Pierre Brossolette, Chilly-Mazarin, France, 91380
Public contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.com
Scientific contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.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	08 April 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	02 April 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate progression free survival (PFS) improvement for cabazitaxel compared to topotecan in subjects with sensitive or resistant/refractory small cell lung cancer following a first line platinum based chemotherapy.

Protection of trial subjects:

Subjects were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time in language and terms appropriate for the subject and considering the local culture. During the course of the trial, subjects were provided with individual subject cards indicating the nature of the trial the subject is participating, contact details and any information needed in the event of a medical emergency.
Collected personal data and human biological samples were processed in compliance with the Sanofi-Aventis Group Personal Data Protection Charter ensuring that the Group abides by the laws governing personal data protection in force in all countries in which it operates.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 March 2012
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	Norway: 5
Country: Number of subjects enrolled	Poland: 13
Country: Number of subjects enrolled	Spain: 10
Country: Number of subjects enrolled	France: 12
Country: Number of subjects enrolled	Germany: 9
Country: Number of subjects enrolled	Greece: 14
Country: Number of subjects enrolled	Hungary: 25
Country: Number of subjects enrolled	Italy: 7
Country: Number of subjects enrolled	Brazil: 4
Country: Number of subjects enrolled	Canada: 15
Country: Number of subjects enrolled	Chile: 2
Country: Number of subjects enrolled	Korea, Republic of: 13
Country: Number of subjects enrolled	Romania: 10
Country: Number of subjects enrolled	Russian Federation: 21
Country: Number of subjects enrolled	Ukraine: 8
Country: Number of subjects enrolled	United States: 11

Worldwide total number of subjects	179
EEA total number of subjects	105

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)	116
From 65 to 84 years	63
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 232 subjects were screened of which 53 were screen failure and 179 were randomized.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cabazitaxel

Arm description:

Cabazitaxel on Day 1 every 3 weeks (21-day cycle) until unacceptable toxicity, disease progression or withdrawal consent.

Arm type	Experimental
Investigational medicinal product name	Cabazitaxel
Investigational medicinal product code	XRP6258
Other name	Jevtana
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Cabazitaxel 25 mg/m^2.

Arm title	Topotecan

Arm description:

Topotecan on Day 1 to Day 5 every 3 weeks (21-Day cycle) until unacceptable toxicity, disease progression or withdrawal consent.

Arm type	Active comparator
Investigational medicinal product name	Topotecan
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Topotecan 1.5 mg/m^2.

Number of subjects in period 1	Cabazitaxel	Topotecan
Started	90	89
Treated	89	88
Completed	85	80
Not completed	5	9
Randomized But Not Treated	1	1

Unspecified	4	8

Baseline characteristics

Reporting groups	
Reporting group title	Cabazitaxel
Reporting group description:	
Cabazitaxel on Day 1 every 3 weeks (21-day cycle) until unacceptable toxicity, disease progression or withdrawal consent.	
Reporting group title	Topotecan
Reporting group description:	
Topotecan on Day 1 to Day 5 every 3 weeks (21-Day cycle) until unacceptable toxicity, disease progression or withdrawal consent.	

Reporting group values	Cabazitaxel	Topotecan	Total
Number of subjects	90	89	179
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	59.9	61.6	
standard deviation	± 9.4	± 10	-
Gender categorical Units: Subjects			
Female	27	27	54
Male	63	62	125
Race Units: Subjects			
Caucasian/White	80	82	162
Black	1	2	3
Asian/Oriental	9	4	13
Other	0	1	1
Ethnicity Units: Subjects			
Hispanic	4	3	7
Not Hispanic	86	86	172
Eastern Cooperative Oncology Group (ECOG) Performance Status			
ECOG criteria: 0: Fully active 1: Ambulatory, carry out work of a light or sedentary nature 2: Ambulatory, capable of all selfcare 3: Capable of limited selfcare, confined to bed or chair more than 50% of waking hours 4: Completely disabled, no selfcare, totally confined to bed or chair 5: Dead			
Units: Subjects			
ECOG criteria: 0	31	17	48
ECOG criteria: 1	59	71	130
ECOG criteria: 2	0	1	1
Primary Tumor Site Units: Subjects			
Lungs	16	20	36

Right Lung	33	43	76
Left Lung	40	26	66
Other: Mediastino-Hilar	1	0	1
Stage at Diagnosis			
Disease stages were decided based on tumor size, lymph nodes and metastasis (as per National Comprehensive Cancer Network guidelines Version 2.2013).			
Units: Subjects			
IIA	1	1	2
IIB	2	1	3
IIIA	2	12	14
IIIB	25	15	40
IV	57	55	112
Unknown	3	5	8
Number of Organs Involved			
Units: organs			
arithmetic mean	3.6	3.8	
standard deviation	± 1.3	± 1.4	-

End points

End points reporting groups

Reporting group title	Cabazitaxel
Reporting group description:	
Cabazitaxel on Day 1 every 3 weeks (21-day cycle) until unacceptable toxicity, disease progression or withdrawal consent.	
Reporting group title	Topotecan
Reporting group description:	
Topotecan on Day 1 to Day 5 every 3 weeks (21-Day cycle) until unacceptable toxicity, disease progression or withdrawal consent.	

Primary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)
End point description:	
PFS was defined as the time interval from the date of randomization to the date of occurrence of the first documented tumor progression or death due to any cause, whichever came first. Median PFS was estimated using the Kaplan-Meier method. Progression was defined using Response Evaluation Criteria in Solid Tumors (RECIST) (version 1.1) as: at least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study or unequivocal progression of existing non-target lesion. In addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of at least 5 millimeter (mm). The appearance of one or more new lesions is also considered progression. Intent-to-treat (ITT) population included all randomized subjects.	
End point type	Primary
End point timeframe:	
Randomization to first tumor progression/clinical deterioration or death (maximum 7.6 months)	

End point values	Cabazitaxel	Topotecan		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	90	89		
Units: months				
median (confidence interval 95%)	1.4 (1.4 to 1.5)	3 (2.7 to 4.1)		

Statistical analyses

Statistical analysis title	Cabazitaxel vs. Topotecan
Statistical analysis description:	
Hazard ratio was estimated using a COX Proportional Hazards regression model, stratifying for brain metastases and LDH level at the time of randomization.	
Comparison groups	Cabazitaxel v Topotecan

Number of subjects included in analysis	179
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.0001 [1]
Method	Stratified Two-Sided Log-Rank Test
Parameter estimate	Cox proportional hazard
Point estimate	2.169
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.563
upper limit	3.01

Notes:

[1] - P-value was calculated from stratified two-sided log-rank test, stratifying for brain metastases and lactate dehydrogenase (LDH) level at the time of randomization.

Secondary: Overall Survival

End point title	Overall Survival

End point description:

Overall survival was defined as the time interval from the date of randomization to the date of death due to any cause. In the absence of confirmation of death, survival time was to be censored at the last date the subject was known to be alive. Median time was estimated by Kaplan-Meier curve. ITT population.

End point type	Secondary

End point timeframe:

From randomization to date of death (maximum 15 months)

End point values	Cabazitaxel	Topotecan		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	90	89		
Units: months				
median (confidence interval 95%)	5.2 (3.38 to 6.11)	6.8 (5.03 to 8.08)		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Rate at Week 12

End point title	Progression Free Rate at Week 12

End point description:

Progression was defined using Response Evaluation Criteria in Solid Tumors (RECIST) (version 1.1) as: at least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study or unequivocal progression of existing non-target lesion. In addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of at least 5 mm. The appearance of one or more new lesions is also considered progression. Death due to disease progression within 12 weeks without radiological documentation of progressive disease was counted as an event. Percentage of subjects who were progression free at week 12 are reported. ITT population.

End point type	Secondary

End point timeframe:

week 12

End point values	Cabazitaxel	Topotecan		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	90	89		
Units: percentage of subjects				
number (confidence interval 95%)	18.9 (11.4 to 28.5)	52.8 (41.9 to 63.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Objective Tumor Response Rate

End point title	Overall Objective Tumor Response Rate

End point description:

Overall objective tumor response was defined as the proportion of subjects with confirmed RECIST 1.1 achieving a complete response (CR) or partial response (PR). CR was defined as disappearance of all target/non-target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to <10 mm. PR was defined as at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters. Percentage of subjects with overall objective tumor response is reported. ITT population.

End point type	Secondary

End point timeframe:

Randomization to disease progression/occurrence (maximum 7.6 months)

End point values	Cabazitaxel	Topotecan		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	90	89		
Units: percentage of subjects				
number (confidence interval 95%)	0 (0 to 4.9)	10.1 (4.5 to 19)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All Adverse Events (AE) were collected from signature of the informed consent form until 30 days after last study treatment administration (maximum 66 weeks) regardless of seriousness or relationship to investigational product.

Adverse event reporting additional description:

Reported AEs and deaths are treatment-emergent that is AEs that developed/worsened and death that occurred during the 'on treatment period' (from the first study treatment administration until 30 days after the last dose of study treatment). Safety population all randomized subjects who received at least one dose of study medication (treated).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups

Reporting group title	Topotecan

Reporting group description:

Topotecan on Day 1 to Day 5 every 3 weeks (21-Day cycle) until unacceptable toxicity, disease progression or withdrawal consent.

Reporting group title	Cabazitaxel

Reporting group description:

Cabazitaxel on Day 1 every 3 weeks (21-day cycle) until unacceptable toxicity, disease progression or withdrawal consent.

Serious adverse events	Topotecan	Cabazitaxel	
Total subjects affected by serious adverse events			
subjects affected / exposed	41 / 88 (46.59%)	36 / 89 (40.45%)	
number of deaths (all causes)	13	12	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour Pain			
subjects affected / exposed	0 / 88 (0.00%)	1 / 89 (1.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 88 (1.14%)	0 / 89 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			

Asthenia			
subjects affected / exposed	2 / 88 (2.27%)	2 / 89 (2.25%)	
occurrences causally related to treatment / all	1 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	0 / 88 (0.00%)	1 / 89 (1.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Generalised Oedema			
subjects affected / exposed	0 / 88 (0.00%)	1 / 89 (1.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 88 (1.14%)	0 / 89 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Performance Status Decreased			
subjects affected / exposed	1 / 88 (1.14%)	0 / 89 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disease Progression			
subjects affected / exposed	4 / 88 (4.55%)	6 / 89 (6.74%)	
occurrences causally related to treatment / all	0 / 4	0 / 6	
deaths causally related to treatment / all	0 / 4	0 / 6	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 88 (1.14%)	1 / 89 (1.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Acute Respiratory Failure			
subjects affected / exposed	0 / 88 (0.00%)	1 / 89 (1.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	

Haemoptysis			
subjects affected / exposed	0 / 88 (0.00%)	1 / 89 (1.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural Effusion			
subjects affected / exposed	0 / 88 (0.00%)	1 / 89 (1.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	0 / 88 (0.00%)	1 / 89 (1.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary Embolism			
subjects affected / exposed	1 / 88 (1.14%)	2 / 89 (2.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary Haemorrhage			
subjects affected / exposed	1 / 88 (1.14%)	0 / 89 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pulmonary Microemboli			
subjects affected / exposed	1 / 88 (1.14%)	0 / 89 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Respiratory Failure			
subjects affected / exposed	2 / 88 (2.27%)	2 / 89 (2.25%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 2	0 / 1	
Respiratory Distress			
subjects affected / exposed	1 / 88 (1.14%)	0 / 89 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			

White Blood Cell Decreased			
subjects affected / exposed	0 / 88 (0.00%)	1 / 89 (1.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Platelet Count Decreased			
subjects affected / exposed	2 / 88 (2.27%)	0 / 89 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutrophil Count Decreased			
subjects affected / exposed	1 / 88 (1.14%)	0 / 89 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood Creatinine Increased			
subjects affected / exposed	1 / 88 (1.14%)	0 / 89 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Craniocerebral Injury			
subjects affected / exposed	1 / 88 (1.14%)	0 / 89 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac disorders			
Pericardial Effusion			
subjects affected / exposed	1 / 88 (1.14%)	2 / 89 (2.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiopulmonary Failure			
subjects affected / exposed	2 / 88 (2.27%)	0 / 89 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	1 / 2	0 / 0	
Nervous system disorders			
Paraparesis			

subjects affected / exposed	0 / 88 (0.00%)	1 / 89 (1.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	0 / 88 (0.00%)	1 / 89 (1.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Convulsion			
subjects affected / exposed	0 / 88 (0.00%)	1 / 89 (1.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sciatica			
subjects affected / exposed	1 / 88 (1.14%)	0 / 89 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Febrile Neutropenia			
subjects affected / exposed	10 / 88 (11.36%)	6 / 89 (6.74%)	
occurrences causally related to treatment / all	10 / 10	6 / 6	
deaths causally related to treatment / all	2 / 2	0 / 0	
Leukopenia			
subjects affected / exposed	1 / 88 (1.14%)	1 / 89 (1.12%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymph Node Pain			
subjects affected / exposed	0 / 88 (0.00%)	1 / 89 (1.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	2 / 88 (2.27%)	2 / 89 (2.25%)	
occurrences causally related to treatment / all	2 / 2	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			

subjects affected / exposed	2 / 88 (2.27%)	0 / 89 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia			
subjects affected / exposed	6 / 88 (6.82%)	1 / 89 (1.12%)	
occurrences causally related to treatment / all	6 / 6	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	10 / 88 (11.36%)	1 / 89 (1.12%)	
occurrences causally related to treatment / all	14 / 14	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Anal Fistula			
subjects affected / exposed	1 / 88 (1.14%)	0 / 89 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal Pain			
subjects affected / exposed	0 / 88 (0.00%)	2 / 89 (2.25%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal Haemorrhage			
subjects affected / exposed	0 / 88 (0.00%)	1 / 89 (1.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal Ulcer Haemorrhage			
subjects affected / exposed	1 / 88 (1.14%)	0 / 89 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 88 (0.00%)	1 / 89 (1.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal Pain			

subjects affected / exposed	0 / 88 (0.00%)	1 / 89 (1.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 88 (0.00%)	1 / 89 (1.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Cutaneous Lupus Erythematosus			
subjects affected / exposed	1 / 88 (1.14%)	0 / 89 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis Allergic			
subjects affected / exposed	1 / 88 (1.14%)	0 / 89 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Urinary Retention			
subjects affected / exposed	0 / 88 (0.00%)	1 / 89 (1.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	0 / 88 (0.00%)	1 / 89 (1.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back Pain			
subjects affected / exposed	0 / 88 (0.00%)	1 / 89 (1.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bronchitis			

subjects affected / exposed	0 / 88 (0.00%)	1 / 89 (1.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative Wound Infection			
subjects affected / exposed	0 / 88 (0.00%)	1 / 89 (1.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	6 / 88 (6.82%)	1 / 89 (1.12%)	
occurrences causally related to treatment / all	0 / 6	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Neutropenic Sepsis			
subjects affected / exposed	1 / 88 (1.14%)	3 / 89 (3.37%)	
occurrences causally related to treatment / all	1 / 1	3 / 3	
deaths causally related to treatment / all	0 / 0	1 / 1	
Neutropenic Infection			
subjects affected / exposed	5 / 88 (5.68%)	4 / 89 (4.49%)	
occurrences causally related to treatment / all	4 / 5	3 / 4	
deaths causally related to treatment / all	1 / 2	2 / 2	
Lung Infection			
subjects affected / exposed	1 / 88 (1.14%)	1 / 89 (1.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium Difficile Colitis			
subjects affected / exposed	0 / 88 (0.00%)	1 / 89 (1.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory Tract Infection			
subjects affected / exposed	0 / 88 (0.00%)	1 / 89 (1.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypokalaemia			

subjects affected / exposed	0 / 88 (0.00%)	1 / 89 (1.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hyponatraemia			
subjects affected / exposed	0 / 88 (0.00%)	3 / 89 (3.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	1 / 88 (1.14%)	0 / 89 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Topotecan	Cabazitaxel	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	74 / 88 (84.09%)	67 / 89 (75.28%)	
Investigations			
Neutrophil Count Decreased			
subjects affected / exposed	6 / 88 (6.82%)	3 / 89 (3.37%)	
occurrences (all)	7	3	
Weight Decreased			
subjects affected / exposed	4 / 88 (4.55%)	7 / 89 (7.87%)	
occurrences (all)	4	7	
Nervous system disorders			
Dizziness			
subjects affected / exposed	5 / 88 (5.68%)	2 / 89 (2.25%)	
occurrences (all)	6	2	
Headache			
subjects affected / exposed	9 / 88 (10.23%)	6 / 89 (6.74%)	
occurrences (all)	16	7	
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	12 / 88 (13.64%)	0 / 89 (0.00%)	
occurrences (all)	15	0	
Neutropenia			

subjects affected / exposed	19 / 88 (21.59%)	2 / 89 (2.25%)	
occurrences (all)	25	2	
Leukopenia			
subjects affected / exposed	6 / 88 (6.82%)	1 / 89 (1.12%)	
occurrences (all)	6	1	
Febrile Neutropenia			
subjects affected / exposed	5 / 88 (5.68%)	4 / 89 (4.49%)	
occurrences (all)	5	4	
Anaemia			
subjects affected / exposed	18 / 88 (20.45%)	4 / 89 (4.49%)	
occurrences (all)	21	4	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	22 / 88 (25.00%)	26 / 89 (29.21%)	
occurrences (all)	24	29	
Asthenia			
subjects affected / exposed	16 / 88 (18.18%)	10 / 89 (11.24%)	
occurrences (all)	20	11	
Non-Cardiac Chest Pain			
subjects affected / exposed	6 / 88 (6.82%)	6 / 89 (6.74%)	
occurrences (all)	7	6	
Pyrexia			
subjects affected / exposed	7 / 88 (7.95%)	4 / 89 (4.49%)	
occurrences (all)	10	4	
Oedema Peripheral			
subjects affected / exposed	5 / 88 (5.68%)	1 / 89 (1.12%)	
occurrences (all)	5	1	
Gastrointestinal disorders			
Abdominal Pain Upper			
subjects affected / exposed	2 / 88 (2.27%)	5 / 89 (5.62%)	
occurrences (all)	2	5	
Abdominal Pain			
subjects affected / exposed	3 / 88 (3.41%)	8 / 89 (8.99%)	
occurrences (all)	3	8	
Vomiting			

subjects affected / exposed	7 / 88 (7.95%)	15 / 89 (16.85%)	
occurrences (all)	7	20	
Stomatitis			
subjects affected / exposed	3 / 88 (3.41%)	8 / 89 (8.99%)	
occurrences (all)	4	8	
Nausea			
subjects affected / exposed	11 / 88 (12.50%)	14 / 89 (15.73%)	
occurrences (all)	14	18	
Diarrhoea			
subjects affected / exposed	9 / 88 (10.23%)	17 / 89 (19.10%)	
occurrences (all)	11	26	
Constipation			
subjects affected / exposed	9 / 88 (10.23%)	8 / 89 (8.99%)	
occurrences (all)	9	8	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	21 / 88 (23.86%)	8 / 89 (8.99%)	
occurrences (all)	21	8	
Cough			
subjects affected / exposed	8 / 88 (9.09%)	10 / 89 (11.24%)	
occurrences (all)	8	11	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	5 / 88 (5.68%)	5 / 89 (5.62%)	
occurrences (all)	5	5	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	6 / 88 (6.82%)	2 / 89 (2.25%)	
occurrences (all)	6	2	
Back Pain			
subjects affected / exposed	5 / 88 (5.68%)	8 / 89 (8.99%)	
occurrences (all)	9	8	
Musculoskeletal Pain			
subjects affected / exposed	5 / 88 (5.68%)	9 / 89 (10.11%)	
occurrences (all)	6	9	
Myalgia			

subjects affected / exposed	0 / 88 (0.00%)	5 / 89 (5.62%)	
occurrences (all)	0	5	
Pain In Extremity			
subjects affected / exposed	6 / 88 (6.82%)	1 / 89 (1.12%)	
occurrences (all)	6	1	
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	13 / 88 (14.77%)	16 / 89 (17.98%)	
occurrences (all)	15	20	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 May 2012	- Changes made following major comments received from study investigators and from Health Authorities or Ethics Committees/International Review Boards further to regulatory submissions of study protocol. - Editorial changes to improve clarity. - Updated the written subject information in order to reflect the changes within the protocol.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported