Clinical trial results:
A randomised Phase II/III study of cabazitaxel versus vinflunine in metastatic or locally advanced transitional cell carcinoma of the urothelium

Summary

EudraCT number	2012-002826-55
Trial protocol	ES NL
Global end of trial date	12 January 2016

Results information

Result version number	v1 (current)
This version publication date	16 February 2018
First version publication date	16 February 2018
Summary attachment (see zip file)	Secavin manuscript Ann Oncol. 2017 Jul 1;28(7):1517-1522. doi: 10.1093/annonc/mdx186. (SECAVIN mdx186.pdf) Secavin Final Study Report (SECAVIN-12 FSR(Version 1.0-16-June-2016).pdf)

Trial information

Trial identification

Sponsor protocol code	SECAVIN-12

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01830231
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	APRO
Sponsor organisation address	Paseo Bonanova, 56 - Bj 2 Barcelona , Barcelona, Spain, 28023
Public contact	Inmaculada Musté, Per a la Recerca Oncològica (APRO), 0034 93248 30 00, oncologia.apro@gmail.com
Scientific contact	Inmaculada Musté, Per a la Recerca Oncològica (APRO), 0034 93248 30 00, oncologia.apro@gmail.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	16 June 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 February 2015
Global end of trial reached?	Yes
Global end of trial date	12 January 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Phase II part:
-efficacy of cabazitaxel compared to vinflunine in terms of improved objective response rate (ORR) of subjects with metastatic or locally advanced previously treated TCCU.
Phase III part:
-efficacy of cabazitaxel compared to vinflunine in terms of improved OS of subjects with metastatic or locally advanced, previously treated TCCU.

Protection of trial subjects:

As per IAC recommendations the phase III part of the study did not go ahead.

Background therapy:

There was not any background therapy

Evidence for comparator:

Vinflunine is a reasonable option for patients with advanced urothelial cancer, and currently is the only second-line treatment approved in monotherapy for adult patients with advanced TCCU after failure of platinum-containing therapy.
In a recent phase III study evaluating vinflunine plus Best Supportive Care (BSC) versus BSC alone as second-line treatment, it revealed moderate activity (ORR, 8.6%) and a clinical benefit with a favourable safety profile. A beneficial effect on survival in favour of vinflunine+BSC vs. BSC was observed (6.9 v 4.3 months), with the difference being statistically significant (P=0.040) in the eligible population. A multivariate Cox analysis adjusting for prognostic factors showed statistically significant effect of vinflunine on OS (P=0.036), reducing the death risk by 23% (HR= 0.77; 95% CI, 0.61 to 0.98).
Cabazitaxel (XRP6258) is a new taxoid, which promotes tubulin assembly in vitro and stabilizes microtubules against cold-induced depolymerization as efficiently as docetaxel. In vitro, cabazitaxel demonstrates cytotoxic activity equivalent to docetaxel. Cabazitaxel demonstrated a broad spectrum of antitumoural activity against advanced human tumour xenografts in mice. Cabazitaxel is active in tumours sensitive to docetaxel. In addition, cabazitaxel demonstrates activity in tumour models insensitive to chemotherapy, including docetaxel. At present, data from clinical studies in patients with urothelial cancer is scarce.

Actual start date of recruitment	01 December 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 5
Country: Number of subjects enrolled	Spain: 65
Worldwide total number of subjects	70
EEA total number of subjects	70

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)	34
From 65 to 84 years	36
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were included from Spain and The Netherlands. Seventy patients had to be included for the phase II part of the study and, if responses were considered as positive by the Independent Assessment Committee, the study would proceed to phase III. FPI was 12 June 2013. LPI was 29 April 2015.

Pre-assignment

Screening details:

Random assignment of treatment was stratified by the presence of 0 versus 1 of the following unfavourable prognostic risk factors:
- ECOG PS 1.
- Anaemia with Hb <10 g/dL.
- Presence of liver metastases.

Despite 70 patients were included, only 44 were evaluable for response (per protocol population)

Pre-assignment period milestones

Number of subjects started	70
Number of subjects completed	70

Period 1

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

Blinding implementation details:

Study was not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Experimental

Arm description:

Cabazitaxel

Arm type	Experimental
Investigational medicinal product name	cabazitaxel
Investigational medicinal product code	XRP6258
Other name	
Pharmaceutical forms	Concentrate and solvent for suspension for injection
Routes of administration	Intravenous use

Dosage and administration details:

Given intravenously once every 21 days.
Cabazitaxel drug products should be administered only by intravenous route. It is supplied as a kit containing one single-use vial of cabazitaxel concentrate for solution for infusion and one single vial of solvent for dilution. The administration of the product requires two dilutions prior to administration.
The recommended infusion duration is one hour. The infusion solution should be used within 8 hours at ambient temperature (including the one hour infusion time) or within a total of 48 hours if refrigerated (including the one hour infusion time).
The infusion solution should be administered at room temperature under normal lighting conditions.
On Day 1 of each cycle, patients will receive cabazitaxel at a dose of 25 mg/m², administered by IV route in 1 hour.
Cycle length for cabazitaxel is 3 weeks. Patients had to be premedicated accordingly.

Arm title	Control arm

Arm description:

Vinflunine. Vinflunine is available as a vinflunine 25 mg/ml concentrate for solution for infusion (sterile

concentrate). Cycle length for vinflunine is 3 weeks (21 days). Before each cycle, adequate monitoring of complete blood counts should be conducted to verify the ANC as neutropaenia is a frequent AR of vinflunine. New cycles of therapy may not begin until ANC ≥1x109/L, platelet count ≥100x109/L, and non-haematological toxicities (except alopecia) have recovered to baseline. On Day 1 of each cycle, patients will receive vinflunine at a dose of 320 mg/m², administered as a 20 minute intravenous infusion. In case of ECOG PS of 1 or PS of 0 and prior pelvic irradiation, or in patients at least 75 years old but less than 80 years, the treatment should be started at the dose of 280 mg/m². In patients 80 years old and beyond, the dose of vinflunine to be given is 250 mg/m² every 3 weeks. In the absence of any haematological toxicity during the first cycle causing treatment delay or dos

Arm type	Active comparator
Investigational medicinal product name	vinflunine
Investigational medicinal product code	
Other name	JAVLOR
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

On Day 1 of each cycle, patients will receive vinflunine at a dose of 320 mg/m², administered as a 20 minute intravenous infusion. In case of ECOG PS of 1 or PS of 0 and prior pelvic irradiation, or in patients at least 75 years old but less than 80 years, the treatment should be started at the dose of 280 mg/m². In patients 80 years old and beyond, the dose of vinflunine to be given is 250 mg/m² every 3 weeks.
In the absence of any haematological toxicity during the first cycle causing treatment delay or dose reduction, the dose will be increased to 320 mg/m² every 3 weeks for the subsequent cycles.

Number of subjects in period 1	Experimental	Control arm
Started	35	35
Completed	35	35

Baseline characteristics

Reporting groups

Reporting group title	Baseline period

Reporting group description: -

Reporting group values	Baseline period	Total	
Number of subjects	70	70	
Age categorical			
Age was presented as mean and median values. Mean age in the cabazitaxel arm was 62.09 (SD 8.43). Median was 64 years (Q1Q3 56, 68). Min was 42 and Max value 77 years. For the vinflunine arm, mean was 64.29, with SD 9.62; median was 66 years, with Q1, Q3 (59, 70), minimum and maximum values were 35 and 80.			
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)	47	47	
From 65-84 years	23	23	
85 years and over	0	0	
Age continuous			
Units: years			
median	65		
standard deviation	± 9.05	-	
Gender categorical			
Units: Subjects			
Female	56	56	
Male	14	14	

Subject analysis sets

Subject analysis set title	Analysis populations
Subject analysis set type	Intention-to-treat

Subject analysis set description:

ITT population included all randomized patients. ITT comprised 35 patients per arm, with median age 64 (cabazitaxel) and 66 years (vinflunine arm), with 28 male and 7 female patients at each arm, and comparable baseline charcteristics in weight, height, body surface and vital signs. All randomized patients had received previously one chemotherapy for advanced disease. Previous radiotherapy was reported for 7 patients (cabazitaxel) and 6 patients (vinflunine arm). Prior surgery was reported for 26 patients (cabazitaxel) and 33 (vinflunine arm). Main prior chemotherapy was cisplatin-gemcitabine, despite 6 patients in the cabazitaxel arm and 14 patients in the vinflunine arm had previously received carboplatin-gemcitabine.

Reporting group values	Analysis populations		
Number of subjects	70		
Age categorical			
Age was presented as mean and median values. Mean age in the cabazitaxel arm was 62.09 (SD 8.43). Median was 64 years (Q1Q3 56, 68). Min was 42 and Max value 77 years. For the vinflunine arm, mean was 64.29, with SD 9.62; median was 66 years, with Q1, Q3 (59, 70), minimum and maximum values were 35 and 80.			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	47		
From 65-84 years	23		
85 years and over	0		
Age continuous			
Units: years			
median	65		
standard deviation	± 9.05		
Gender categorical			
Units: Subjects			
Female	56		
Male	14		

End points

End points reporting groups

Reporting group title	Experimental
Reporting group description:	
Cabazitaxel	
Reporting group title	Control arm
Reporting group description:	
Vinflunine. Vinflunine is available as a vinflunine 25 mg/ml concentrate for solution for infusion (sterile concentrate). Cycle length for vinflunine is 3 weeks (21 days). Before each cycle, adequate monitoring of complete blood counts should be conducted to verify the ANC as neutropaenia is a frequent AR of vinflunine. New cycles of therapy may not begin until ANC ≥1x109/L, platelet count ≥100x109/L, and non-haematological toxicities (except alopecia) have recovered to baseline. On Day 1 of each cycle, patients will receive vinflunine at a dose of 320 mg/m², administered as a 20 minute intravenous infusion. In case of ECOG PS of 1 or PS of 0 and prior pelvic irradiation, or in patients at least 75 years old but less than 80 years, the treatment should be started at the dose of 280 mg/m². In patients 80 years old and beyond, the dose of vinflunine to be given is 250 mg/m² every 3 weeks. In the absence of any haematological toxicity during the first cycle causing treatment delay or dos	
Subject analysis set title	Analysis populations
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
ITT population included all randomized patients. ITT comprised 35 patients per arm, with median age 64 (cabazitaxel) and 66 years (vinflunine arm), with 28 male and 7 female patients at each arm, and comparable baseline charcteristics in weight, height, body surface and vital signs. All randomized patients had received previously one chemotherapy for advanced disease. Previous radiotherapy was reported for 7 patients (cabazitaxel) and 6 patients (vinflunine arm). Prior surgery was reported for 26 patients (cabazitaxel) and 33 (vinflunine arm). Main prior chemotherapy was cisplatin-gemcitabine, despite 6 patients in the cabazitaxel arm and 14 patients in the vinflunine arm had previously received carboplatin-gemcitabine.	

Primary: change in response rate

End point title	change in response rate
End point description:	
The ORR and best overall responses were analyzed taking into account RECIST 1.1 criteria. There were 4 patients with partial response in the cabazitaxel arm and 8 patients with partial response in the vinflunine arm.	
End point type	Primary
End point timeframe:	
Responses were collected until each patient developed progressive disease	

End point values	Experimental	Control arm	Analysis populations	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	35[1]	35[2]	70[3]	
Units: number of partial and complete responses				
Partial Response	4	8	12	
Complete Response	0	0	0	
Stable disease	11	14	25	
Progressive disease	15	11	26	

Notes:
[1] - Cabazitaxel arm
[2] - Vinflunine arm
[3] - ITT population

Statistical analyses

Statistical analysis title	Progression free survival
Statistical analysis description:	
PFs was defined as the time from randomization date to objective tumor progression or death	
Comparison groups	Experimental v Control arm v Analysis populations
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	equivalence[4]
P-value	< 0.05 [5]
Method	Regression, Cox
Parameter estimate	Cox proportional hazard
Point estimate	1.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.0931
upper limit	3.165
Variability estimate	Standard deviation

Notes:
[4] - Number of patients with event was 32 for the cabazitaxel arm versus 29 for the vinflunine arm. Median PFS was 1.78 months for the cabazitaxel arm versus 2.89 for the vinflunine arm.
[5] - p was 0.0221

Secondary: change in PFS

End point title	change in PFS
End point description:	
Median PFS was 1.78 months for cabazitaxel versus 2.89 months for vinflunine	
End point type	Secondary
End point timeframe:	
time from randomization till death or progressive disease	

End point values	Experimental	Control arm	Analysis populations	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	35[6]	35[7]	35[8]	
Units: months				
median (confidence interval 95%)				
dead	1.78 (1.35 to 4.34)	2.89 (1.45 to 8.68)	1.78 (1.35 to 4.34)	
alive	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	

Notes:

[6] - cabazitaxel arm

[7] - vinflunine arm

[8] - cabazitaxel arm

Statistical analyses

No statistical analyses for this end point

Secondary: Change in OS

End point title	Change in OS

End point description:

Overall survival(OS), is defined as the time from randomization date to death date, due to any cause. For the OS analysis, patients who were lost to follow-up were censored at the date of last contact.

End point type	Secondary

End point timeframe:

From randomization to death

End point values	Experimental	Control arm	Analysis populations	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	35[9]	35[10]		
Units: months				
median (confidence interval 95%)	5.49 (3.65 to 11.74)	8.35 (5.03 to 13.87)	5.49 (3.65 to 11.74)	

Notes:

[9] - cabazitaxel arm

[10] - vinflunine arm

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From randomization date to the last contact date	
Adverse event reporting additional description:	
Median follow up time was 13.81 months for cazabitaxel versus 17.88 months for vinflunine arm	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	18

Reporting groups	
Reporting group title	Safety population
Reporting group description:	
All exposed subjects	
Reporting group title	cabazitaxel
Reporting group description:	
Patients in cabazitaxel arm	
Reporting group title	vinflunine arm
Reporting group description:	
Patients on vinflunine arm	

Serious adverse events	Safety population	cabazitaxel	vinflunine arm
Total subjects affected by serious adverse events			
subjects affected / exposed	38 / 70 (54.29%)	20 / 35 (57.14%)	18 / 35 (51.43%)
number of deaths (all causes)	4	4	0
number of deaths resulting from adverse events	4	1	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
tumor pain back			
subjects affected / exposed	1 / 70 (1.43%)	1 / 35 (2.86%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
fever			
subjects affected / exposed	2 / 70 (2.86%)	1 / 35 (2.86%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	2 / 2	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
malaise			

subjects affected / exposed	1 / 70 (1.43%)	0 / 35 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	1 / 70 (1.43%)	1 / 35 (2.86%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
disease progression			
subjects affected / exposed	1 / 70 (1.43%)	1 / 35 (2.86%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
general malaise			
subjects affected / exposed	2 / 70 (2.86%)	1 / 35 (2.86%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	2 / 2	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
clinical deterioration			
subjects affected / exposed	1 / 70 (1.43%)	1 / 35 (2.86%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
pain pelvis			
subjects affected / exposed	1 / 70 (1.43%)	1 / 35 (2.86%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
respiratory insuficience			
subjects affected / exposed	1 / 70 (1.43%)	1 / 35 (2.86%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COPD worsening			
subjects affected / exposed	1 / 70 (1.43%)	0 / 35 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Injury, poisoning and procedural complications			
opioid intoxication			
subjects affected / exposed	1 / 70 (1.43%)	1 / 35 (2.86%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
flutter auricular			
subjects affected / exposed	1 / 70 (1.43%)	0 / 35 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
paroximal supraventricular tachycardia			
subjects affected / exposed	1 / 70 (1.43%)	1 / 35 (2.86%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	1 / 70 (1.43%)	1 / 35 (2.86%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
myocard infarction			
subjects affected / exposed	1 / 70 (1.43%)	1 / 35 (2.86%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Nervous system disorders			
low extremities muscle weakness			
subjects affected / exposed	1 / 70 (1.43%)	0 / 35 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
myelum compression			
subjects affected / exposed	1 / 70 (1.43%)	1 / 35 (2.86%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			

subjects affected / exposed	1 / 70 (1.43%)	0 / 35 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
low awareness level due to progression brain disease			
subjects affected / exposed	1 / 70 (1.43%)	0 / 35 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Blood and lymphatic system disorders			
anemia			
subjects affected / exposed	1 / 70 (1.43%)	1 / 35 (2.86%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
afebrile neutropenia			
subjects affected / exposed	5 / 70 (7.14%)	0 / 35 (0.00%)	5 / 35 (14.29%)
occurrences causally related to treatment / all	5 / 5	0 / 0	5 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
febrile neutropenia			
subjects affected / exposed	7 / 70 (10.00%)	3 / 35 (8.57%)	4 / 35 (11.43%)
occurrences causally related to treatment / all	7 / 7	3 / 3	4 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	1 / 70 (1.43%)	1 / 35 (2.86%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	4 / 70 (5.71%)	3 / 35 (8.57%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	4 / 4	3 / 3	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Constipation	Additional description: Constipation occurred in 24 patients in vinflunine arm		
subjects affected / exposed	4 / 70 (5.71%)	0 / 35 (0.00%)	4 / 35 (11.43%)
occurrences causally related to treatment / all	4 / 4	0 / 0	4 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

diarrhea			
subjects affected / exposed	1 / 70 (1.43%)	1 / 35 (2.86%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
intestinal suboclusion			
subjects affected / exposed	1 / 70 (1.43%)	0 / 35 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
intestinal suboclussion			
subjects affected / exposed	1 / 70 (1.43%)	0 / 35 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
hematuria			
subjects affected / exposed	2 / 70 (2.86%)	2 / 35 (5.71%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
renal failure			
subjects affected / exposed	1 / 70 (1.43%)	1 / 35 (2.86%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
acute kidney failure			
subjects affected / exposed	1 / 70 (1.43%)	1 / 35 (2.86%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
pain in left lower extremity			
subjects affected / exposed	1 / 70 (1.43%)	0 / 35 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
uncontrolled bone pain			
subjects affected / exposed	1 / 70 (1.43%)	0 / 35 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Infections and infestations			
respiratory infection			
subjects affected / exposed	2 / 70 (2.86%)	0 / 35 (0.00%)	2 / 35 (5.71%)
occurrences causally related to treatment / all	2 / 2	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
urinary infection			
subjects affected / exposed	4 / 70 (5.71%)	4 / 35 (11.43%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	4 / 4	4 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
urinary sepsis			
subjects affected / exposed	1 / 70 (1.43%)	0 / 35 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
erysipelas			
subjects affected / exposed	1 / 70 (1.43%)	0 / 35 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
abscess			
subjects affected / exposed	1 / 70 (1.43%)	1 / 35 (2.86%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
wound infection			
subjects affected / exposed	1 / 70 (1.43%)	1 / 35 (2.86%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pneumonia			
subjects affected / exposed	1 / 70 (1.43%)	1 / 35 (2.86%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 70 (1.43%)	1 / 35 (2.86%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
neutropenia urosepsis			

subjects affected / exposed	1 / 70 (1.43%)	1 / 35 (2.86%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Metabolism and nutrition disorders			
hyponatremia			
subjects affected / exposed	1 / 70 (1.43%)	0 / 35 (0.00%)	1 / 35 (2.86%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 3 %

Non-serious adverse events	Safety population	cabazitaxel	vinflunine arm
Total subjects affected by non-serious adverse events			
subjects affected / exposed	70 / 70 (100.00%)	35 / 35 (100.00%)	35 / 35 (100.00%)
General disorders and administration site conditions			
decreased apetite			
subjects affected / exposed	23 / 70 (32.86%)	11 / 35 (31.43%)	12 / 35 (34.29%)
occurrences (all)	23	11	12
fatigue			
subjects affected / exposed	25 / 70 (35.71%)	11 / 35 (31.43%)	14 / 35 (40.00%)
occurrences (all)	25	11	14
asthenia			
subjects affected / exposed	22 / 70 (31.43%)	8 / 35 (22.86%)	14 / 35 (40.00%)
occurrences (all)	22	8	14
pyrexia			
subjects affected / exposed	18 / 70 (25.71%)	8 / 35 (22.86%)	10 / 35 (28.57%)
occurrences (all)	18	8	10
febrile neutropenia			
subjects affected / exposed	10 / 70 (14.29%)	7 / 35 (20.00%)	3 / 35 (8.57%)
occurrences (all)	10	7	3
Blood and lymphatic system disorders			
neutropenia			
subjects affected / exposed	13 / 70 (18.57%)	5 / 35 (14.29%)	8 / 35 (22.86%)
occurrences (all)	13	5	8
anemia			

subjects affected / exposed	12 / 70 (17.14%)	9 / 35 (25.71%)	3 / 35 (8.57%)
occurrences (all)	12	9	3
Gastrointestinal disorders			
Constipation	Additional description: 30 patients had constipation, 6 in cabazitaxel arm and 24 in vinflunine arm		
subjects affected / exposed	70 / 70 (100.00%)	35 / 35 (100.00%)	35 / 35 (100.00%)
occurrences (all)	70	35	35
nausea			
subjects affected / exposed	23 / 70 (32.86%)	7 / 35 (20.00%)	16 / 35 (45.71%)
occurrences (all)	23	7	16
diarrhea			
subjects affected / exposed	18 / 70 (25.71%)	13 / 35 (37.14%)	5 / 35 (14.29%)
occurrences (all)	18	13	5
vomiting			
subjects affected / exposed	11 / 70 (15.71%)	4 / 35 (11.43%)	7 / 35 (20.00%)
occurrences (all)	11	4	7
mucosal inflammation			
subjects affected / exposed	9 / 70 (12.86%)	2 / 35 (5.71%)	7 / 35 (20.00%)
occurrences (all)	9	2	7
Alopecia			
subjects affected / exposed	8 / 70 (11.43%)	3 / 35 (8.57%)	5 / 35 (14.29%)
occurrences (all)	8	3	5
Abdominal pain			
subjects affected / exposed	8 / 70 (11.43%)	2 / 35 (5.71%)	6 / 35 (17.14%)
occurrences (all)	8	2	6
Respiratory, thoracic and mediastinal disorders			
Respiratory tract infection			
subjects affected / exposed	6 / 70 (8.57%)	1 / 35 (2.86%)	5 / 35 (14.29%)
occurrences (all)	6	1	5
dyspnea			
subjects affected / exposed	6 / 70 (8.57%)	2 / 35 (5.71%)	4 / 35 (11.43%)
occurrences (all)	6	2	4
Renal and urinary disorders			
urinary tract infection			
subjects affected / exposed	12 / 70 (17.14%)	9 / 35 (25.71%)	3 / 35 (8.57%)
occurrences (all)	12	9	3
Musculoskeletal and connective tissue			

disorders			
back pain			
subjects affected / exposed	8 / 70 (11.43%)	5 / 35 (14.29%)	3 / 35 (8.57%)
occurrences (all)	8	5	3
Musculoskeletal pain			
subjects affected / exposed	7 / 70 (10.00%)	4 / 35 (11.43%)	3 / 35 (8.57%)
occurrences (all)	7	4	3
myalgia			
subjects affected / exposed	6 / 70 (8.57%)	0 / 35 (0.00%)	6 / 35 (17.14%)
occurrences (all)	6	0	6

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 July 2013	Amendment 1
03 September 2014	Amendment 2
30 November 2015	Amendment 3

Notes:

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.

Study was finished after phase II part showed that cabazitaxel was not better than vinflunine in terms of ORR and PFS

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/28419193