



## 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)<br>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:

| <b>Subjects enrolled per age group</b>    |    |
|-------------------------------------------|----|
| 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          |
| <b>Arm title</b>             | 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/m<sup>2</sup>, administered by IV route in 1 hour.

Cycle length for cabazitaxel is 3 weeks. Patients had to be premedicated accordingly.

|                  |             |
|------------------|-------------|
| <b>Arm title</b> | 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  $\geq 1 \times 10^9/L$ , platelet count  $\geq 100 \times 10^9/L$ , 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/m<sup>2</sup>, 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/m<sup>2</sup>. In patients 80 years old and beyond, the dose of vinflunine to be given is 250 mg/m<sup>2</sup> 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/m<sup>2</sup>, 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/m<sup>2</sup>. In patients 80 years old and beyond, the dose of vinflunine to be given is 250 mg/m<sup>2</sup> 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/m<sup>2</sup> every 3 weeks for the subsequent cycles.

| <b>Number of subjects in period 1</b> | 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 characteristics 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<br>(gestational age < 37 wks)                                                                                                                                                                                                                                                               | 0                    |  |  |
| Newborns (0-27 days)                                                                                                                                                                                                                                                                                                | 0                    |  |  |
| Infants and toddlers (28 days-23<br>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 $\geq 1 \times 10^9/L$ , platelet count $\geq 100 \times 10^9/L$ , 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/m <sup>2</sup> , 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/m <sup>2</sup> . In patients 80 years old and beyond, the dose of vinflunine to be given is 250 mg/m <sup>2</sup> 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 characteristics 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 <sup>[1]</sup> | 35 <sup>[2]</sup> | 70 <sup>[3]</sup>    |  |
| 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

|                                                                                             |                                                   |
|---------------------------------------------------------------------------------------------|---------------------------------------------------|
| <b>Statistical analysis title</b>                                                           | 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 <sup>[4]</sup>                        |
| P-value                                                                                     | < 0.05 <sup>[5]</sup>                             |
| 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 <sup>[6]</sup>   | 35 <sup>[7]</sup>   | 35 <sup>[8]</sup>    |  |
| 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 <sup>[9]</sup>    | 35 <sup>[10]</sup>   |                      |  |
| 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 cabazitaxel 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 insufficiency                       |                |                |                |
| 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          |
| paroxysmal 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 subocclusion                         |                |                |                |
| 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 subocclusion                         |                |                |                |
| 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 appetite                                    |                   |                   |                   |
| 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<br>occurrences (all)                                | 12 / 70 (17.14%)<br>12                                                                              | 9 / 35 (25.71%)<br>9    | 3 / 35 (8.57%)<br>3     |
| Gastrointestinal disorders                                                      |                                                                                                     |                         |                         |
| Constipation                                                                    | Additional description: 30 patients had constipation, 6 in cabazitaxel arm and 24 in vinflunine arm |                         |                         |
| subjects affected / exposed<br>occurrences (all)                                | 70 / 70 (100.00%)<br>70                                                                             | 35 / 35 (100.00%)<br>35 | 35 / 35 (100.00%)<br>35 |
| nausea<br>subjects affected / exposed<br>occurrences (all)                      | 23 / 70 (32.86%)<br>23                                                                              | 7 / 35 (20.00%)<br>7    | 16 / 35 (45.71%)<br>16  |
| diarrhea<br>subjects affected / exposed<br>occurrences (all)                    | 18 / 70 (25.71%)<br>18                                                                              | 13 / 35 (37.14%)<br>13  | 5 / 35 (14.29%)<br>5    |
| vomiting<br>subjects affected / exposed<br>occurrences (all)                    | 11 / 70 (15.71%)<br>11                                                                              | 4 / 35 (11.43%)<br>4    | 7 / 35 (20.00%)<br>7    |
| mucosal inflammation<br>subjects affected / exposed<br>occurrences (all)        | 9 / 70 (12.86%)<br>9                                                                                | 2 / 35 (5.71%)<br>2     | 7 / 35 (20.00%)<br>7    |
| Alopecia<br>subjects affected / exposed<br>occurrences (all)                    | 8 / 70 (11.43%)<br>8                                                                                | 3 / 35 (8.57%)<br>3     | 5 / 35 (14.29%)<br>5    |
| Abdominal pain<br>subjects affected / exposed<br>occurrences (all)              | 8 / 70 (11.43%)<br>8                                                                                | 2 / 35 (5.71%)<br>2     | 6 / 35 (17.14%)<br>6    |
| Respiratory, thoracic and mediastinal disorders                                 |                                                                                                     |                         |                         |
| Respiratory tract infection<br>subjects affected / exposed<br>occurrences (all) | 6 / 70 (8.57%)<br>6                                                                                 | 1 / 35 (2.86%)<br>1     | 5 / 35 (14.29%)<br>5    |
| dyspnea<br>subjects affected / exposed<br>occurrences (all)                     | 6 / 70 (8.57%)<br>6                                                                                 | 2 / 35 (5.71%)<br>2     | 4 / 35 (11.43%)<br>4    |
| Renal and urinary disorders                                                     |                                                                                                     |                         |                         |
| urinary tract infection<br>subjects affected / exposed<br>occurrences (all)     | 12 / 70 (17.14%)<br>12                                                                              | 9 / 35 (25.71%)<br>9    | 3 / 35 (8.57%)<br>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:

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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.

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

Notes:

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### Online references

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