



Clinical trial results:

A randomized phase II trial of metronomic oral vinorelbine plus cyclophosphamide and capecitabine (VEX) versus weekly paclitaxel as first or second-line treatment in patients with ER-positive/HER2-negative advanced or metastatic breast cancer

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2016-002200-39 |
| Trial protocol | IT |
| Global end of trial date | 23 November 2022 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 29 March 2024 |
| First version publication date | 29 March 2024 |

Trial information

Trial identification

| | |
|-----------------------|-------------|
| Sponsor protocol code | IBCSG 54-16 |
|-----------------------|-------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02954055 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | ETOP IBCSG Partners Foundation |
| Sponsor organisation address | Effingerstrasse 33, Bern, Switzerland, 3008 |
| Public contact | ETOP IBCSG Partners Foundation, ETOP IBCSG Partners Foundation, +41 31 511 94 00, ibcsg-regulatory@etop.ibcsg.org |
| Scientific contact | ETOP IBCSG Partners Foundation, ETOP IBCSG Partners Foundation, +41 31 511 94 00, ibcsg-regulatory@etop.ibcsg.org |

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 | 04 December 2021 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 17 November 2021 |
| Global end of trial reached? | Yes |
| Global end of trial date | 23 November 2022 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

To assess efficacy, as measured by the time to treatment failure (TTF), of the first-line combination treatment with vinorelbine, cyclophosphamide and capecitabine (VEX) in comparison with paclitaxel monotherapy in ER+/HER2-, metastatic or locally advanced breast cancer patients, who have progressed under previous endocrine therapy.

Protection of trial subjects:

Participating institutions' ethics committees or Institutional Review Boards approved the trial according to local laws and regulations. All patients gave written informed consent, and the trial was performed in compliance with the Helsinki Declaration. The Data Safety and Monitoring Board reviewed the data from this research throughout the study.

Background therapy: -

Evidence for comparator: -

| | |
|---|-------------------|
| Actual start date of recruitment | 13 September 2017 |
| 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 | Italy: 140 |
| Worldwide total number of subjects | 140 |
| EEA total number of subjects | 140 |

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) | 91 |
| From 65 to 84 years | 49 |

| | |
|-------------------|---|
| 85 years and over | 0 |
|-------------------|---|

Subject disposition

Recruitment

Recruitment details:

METEORA was activated on 13 February 2017. METEORA enrolled 140 patients in 15 centers in Italy between 13 September 2017 and 14 January 2021

Pre-assignment

Screening details:

Written Informed Consent (IC) was signed and dated by the patient and the Investigator prior to starting screening procedures and randomization.

Period 1

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

Arms

| | |
|------------------------------|------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Paclitaxel |

Arm description:

Paclitaxel 90 mg/m² days 1, 8, 15 q4weeks. Patients will continue to receive assigned treatment until progression or lack of tolerability.

| | |
|--|---------------------------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Paclitaxel |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Paclitaxel 90 mg/m² i.v. days 1, 8, 15 every 4 weeks, according to standard local practice

| | |
|------------------|----------------|
| Arm title | Metronomic VEX |
|------------------|----------------|

Arm description:

Cyclophosphamide 50 mg orally once daily continuously, capecitabine 500 mg, orally 3 times a day (1500 mg/day) continuously, vinorelbine 40 mg orally days 1, 3, 5 each week continuously. Patients will continue to receive assigned treatment until progression or lack of tolerability.

Cyclophosphamide: Arm B

Capecitabine: Arm B

Vinorelbine: Arm B

| | |
|--|------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Cyclophosphamide |
| Investigational medicinal product code | |
| Other name | Endoxan Baxter |
| Pharmaceutical forms | Coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Cyclophosphamide 50 mg orally once daily around 9am

| | |
|--|--------------------|
| Investigational medicinal product name | Capecitabine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |

| | |
|--|-------------|
| Routes of administration | Oral use |
| Dosage and administration details: | |
| Capecitabine 500 mg, orally 3 times a day (total 1500 mg/day) within 30 minutes after meals (breakfast, lunch, dinner) | |
| Investigational medicinal product name | Vinorelbine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

Vinorelbine 40 mg orally days 1, 3, 5 each week (Monday, Wednesday, Friday) after lunch

| Number of subjects in period 1 | Paclitaxel | Metronomic VEX |
|---------------------------------------|------------|----------------|
| Started | 69 | 71 |
| Completed | 63 | 70 |
| Not completed | 6 | 1 |
| Did not initiate therapy | 6 | 1 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|------------|
| Reporting group title | Paclitaxel |
|-----------------------|------------|

Reporting group description:

Paclitaxel 90 mg/m² days 1, 8, 15 q4weeks. Patients will continue to receive assigned treatment until progression or lack of tolerability.

| | |
|-----------------------|----------------|
| Reporting group title | Metronomic VEX |
|-----------------------|----------------|

Reporting group description:

Cyclophosphamide 50 mg orally once daily continuously, capecitabine 500 mg, orally 3 times a day (1500 mg/day) continuously, vinorelbine 40 mg orally days 1, 3, 5 each week continuously. Patients will continue to receive assigned treatment until progression or lack of tolerability.

Cyclophosphamide: Arm B

Capecitabine: Arm B

Vinorelbine: Arm B

| Reporting group values | Paclitaxel | Metronomic VEX | Total |
|---------------------------------------|------------|----------------|-------|
| Number of subjects | 69 | 71 | 140 |
| Age categorical Units: Subjects | | | |
| Adults (18-64 years) | 43 | 48 | 91 |
| From 65-84 years | 26 | 23 | 49 |
| Gender categorical Units: Subjects | | | |
| Female | 69 | 71 | 140 |
| Male | 0 | 0 | 0 |

Subject analysis sets

| | |
|----------------------------|--------------------------------|
| Subject analysis set title | Analysis Population Paclitaxel |
|----------------------------|--------------------------------|

| | |
|---------------------------|--------------------|
| Subject analysis set type | Intention-to-treat |
|---------------------------|--------------------|

Subject analysis set description:

- Efficacy analysis population: All randomized patients who receive at least one dose of trial treatment.
- Safety population: All randomized patients who receive at least one dose of trial treatment will be included in assessments of safety and tolerability.
(thus the two populations are the same)

| | |
|----------------------------|-------------------------|
| Subject analysis set title | Analysis Population VEX |
|----------------------------|-------------------------|

| | |
|---------------------------|--------------------|
| Subject analysis set type | Intention-to-treat |
|---------------------------|--------------------|

Subject analysis set description:

- Efficacy analysis population: All randomized patients who receive at least one dose of trial treatment.
- Safety population: All randomized patients who receive at least one dose of trial treatment will be included in assessments of safety and tolerability.
(thus the two populations are the same)

| Reporting group values | Analysis Population Paclitaxel | Analysis Population VEX | |
|------------------------------------|--------------------------------|-------------------------|--|
| Number of subjects | 63 | 70 | |
| Age categorical Units: Subjects | | | |
| Adults (18-64 years) | 41 | 47 | |

| | | | |
|------------------|----|----|--|
| From 65-84 years | 22 | 23 | |
|------------------|----|----|--|

| | | | |
|---------------------------------------|----|----|--|
| Gender categorical Units: Subjects | | | |
| Female | 63 | 70 | |
| Male | 0 | 0 | |

End points

End points reporting groups

| | |
|-----------------------|------------|
| Reporting group title | Paclitaxel |
|-----------------------|------------|

Reporting group description:

Paclitaxel 90 mg/m² days 1, 8, 15 q4weeks. Patients will continue to receive assigned treatment until progression or lack of tolerability.

| | |
|-----------------------|----------------|
| Reporting group title | Metronomic VEX |
|-----------------------|----------------|

Reporting group description:

Cyclophosphamide 50 mg orally once daily continuously, capecitabine 500 mg, orally 3 times a day (1500 mg/day) continuously, vinorelbine 40 mg orally days 1, 3, 5 each week continuously. Patients will continue to receive assigned treatment until progression or lack of tolerability.

Cyclophosphamide: Arm B

Capecitabine: Arm B

Vinorelbine: Arm B

| | |
|----------------------------|--------------------------------|
| Subject analysis set title | Analysis Population Paclitaxel |
|----------------------------|--------------------------------|

| | |
|---------------------------|--------------------|
| Subject analysis set type | Intention-to-treat |
|---------------------------|--------------------|

Subject analysis set description:

- Efficacy analysis population: All randomized patients who receive at least one dose of trial treatment.
- Safety population: All randomized patients who receive at least one dose of trial treatment will be included in assessments of safety and tolerability.
(thus the two populations are the same)

| | |
|----------------------------|-------------------------|
| Subject analysis set title | Analysis Population VEX |
|----------------------------|-------------------------|

| | |
|---------------------------|--------------------|
| Subject analysis set type | Intention-to-treat |
|---------------------------|--------------------|

Subject analysis set description:

- Efficacy analysis population: All randomized patients who receive at least one dose of trial treatment.
- Safety population: All randomized patients who receive at least one dose of trial treatment will be included in assessments of safety and tolerability.
(thus the two populations are the same)

Primary: Time to Treatment Failure (TTF)

| | |
|-----------------|---------------------------------|
| End point title | Time to Treatment Failure (TTF) |
|-----------------|---------------------------------|

End point description:

Efficacy and tolerability, measured by time to treatment failure, of metronomic oral vinorelbine plus cyclophosphamide and capecitabine (VEX) versus weekly paclitaxel, using an intent-to-treat analysis approach.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Assessed at the start of every 4-week (28-day) treatment cycle from randomization to the end of treatment date or discontinuation; median follow-up was 29 months, with a minimum of 0.2 months and maximum of 48.5 months.

| End point values | Analysis Population Paclitaxel | Analysis Population VEX | | |
|-----------------------------|--------------------------------|-------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 63 | 70 | | |
| Units: month | | | | |
| median (standard error) | 5.7 (± 0.06) | 8.3 (± 0.06) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Statistical analysis primary endpoint |
| Comparison groups | Analysis Population Paclitaxel v Analysis Population VEX |
| Number of subjects included in analysis | 133 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.008 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.61 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.42 |
| upper limit | 0.88 |

Secondary: Disease Control

| | |
|--|-----------------|
| End point title | Disease Control |
| End point description: | |
| Defined as best overall response of complete response (CR) or partial response (PR), or stable disease (SD) (or non-CR/non-PD in the case of non-measurable disease only) lasting for at least 24 weeks (at least 2 scans), measured from randomization until first documentation of progressive disease. Best overall response was defined as best response recorded from randomization across all time points until disease progression. Confirmation of partial or complete response by an additional scan was not requested in this trial. Disease response and progression were assessed according to the revised Response Evaluation Criteria in Solid Tumors (RECIST version 1.1) | |
| End point type | Secondary |
| End point timeframe: | |
| Tumor measurements were assessed at baseline, and every 12 weeks (\pm 2 weeks) from randomization until first disease progression on the basis of clinical and radiological tumor assessments, on average approximately 9 months. | |

| End point values | Analysis Population Paclitaxel | Analysis Population VEX | | |
|------------------------------------|--------------------------------|-------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 63 | 70 | | |
| Units: Participants | | | | |
| Complete response (CR) | 1 | 1 | | |
| Partial response (PR) | 18 | 22 | | |
| Stable disease (SD)/ non-CR/non-PD | 25 | 32 | | |
| Progressive disease | 18 | 11 | | |

| | | | | |
|---------------|---|---|--|--|
| Not evaluable | 1 | 4 | | |
|---------------|---|---|--|--|

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS)

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|-----------------|---------------------------------|
| End point title | Progression Free Survival (PFS) |
|-----------------|---------------------------------|

End point description:

PFS was defined as time from randomization until documented disease progression according to Response Evaluation Criteria in Solid Tumors (RECIST 1.1) criteria or death, whichever occurred first; the death must have occurred within an interval of time corresponding to the interval of tumor re-evaluations. For patients without progression, follow-up was censored at the date of last disease assessment.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Tumor measurements were assessed at baseline, and every 12 weeks (\pm 2 weeks) from randomization until first disease progression on the basis of clinical and radiological tumor assessments, on average approximately 9 months.

| End point values | Analysis Population Paclitaxel | Analysis Population VEX | | |
|-----------------------------|--------------------------------|-------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 63 | 70 | | |
| Units: month | | | | |
| median (standard error) | 6.9 (\pm 0.06) | 11.1 (\pm 0.05) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

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|-----------------|-----------------------|
| End point title | Overall Survival (OS) |
|-----------------|-----------------------|

End point description:

Overall survival from time of randomisation will be summarised for each treatment group.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From day 1 of cycle 1 until death from any cause (censored at date of last assessment of vital status for patients lost to follow up), assessed up to 36 months from the enrollment of the first patient.

| End point values | Analysis Population Paclitaxel | Analysis Population VEX | | |
|-----------------------------|--------------------------------------|----------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 63 | 70 | | |
| Units: month | | | | |
| median (standard error) | 33.7 (± 0.03) | 29.5 (± 0.03) | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events (AEs) were collected from the first dose of trial medication, at day 1 of every treatment cycle, until 28 days after all treatment discontinuation (end of treatment visit), regardless of whether it is considered related to a medication.

Adverse event reporting additional description:

AEs were collected from the first dose of trial medication until 28 days after all treatment discontinuation (EOT visit), regardless of whether it is considered related to a medication. The main criterion for tolerability is the occurrence of toxicities and adverse events.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|--------------------|-----------|
| Dictionary name | NCI CTCAE |
| Dictionary version | 4.0 |

Reporting groups

| | |
|-----------------------|--------------------------------|
| Reporting group title | Analysis Population Paclitaxel |
|-----------------------|--------------------------------|

Reporting group description: -

| | |
|-----------------------|-------------------------|
| Reporting group title | Analysis Population VEX |
|-----------------------|-------------------------|

Reporting group description: -

| Serious adverse events | Analysis Population Paclitaxel | Analysis Population VEX | |
|---|--------------------------------|-------------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 18 / 63 (28.57%) | 31 / 70 (44.29%) | |
| number of deaths (all causes) | 1 | 3 | |
| number of deaths resulting from adverse events | | | |
| Investigations | | | |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 8 / 63 (12.70%) | 20 / 70 (28.57%) | |
| occurrences causally related to treatment / all | 13 / 13 | 28 / 28 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 3 / 70 (4.29%) | |
| occurrences causally related to treatment / all | 0 / 0 | 4 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 2 / 70 (2.86%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Alkaline phosphatase increased | | | |

| | | | |
|--|----------------|------------------|--|
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 70 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lymphocyte count decreased | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 70 (1.43%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| White blood cell decreased | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 12 / 70 (17.14%) | |
| occurrences causally related to treatment / all | 0 / 1 | 12 / 12 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Pulmonary valve disease | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 70 (1.43%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Supraventricular tachycardia | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 70 (1.43%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Peripheral sensory neuropathy | | | |
| subjects affected / exposed | 6 / 63 (9.52%) | 0 / 70 (0.00%) | |
| occurrences causally related to treatment / all | 8 / 8 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 2 / 63 (3.17%) | 5 / 70 (7.14%) | |
| occurrences causally related to treatment / all | 2 / 2 | 6 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |

| | | | |
|---|----------------|----------------|--|
| subjects affected / exposed | 0 / 63 (0.00%) | 4 / 70 (5.71%) | |
| occurrences causally related to treatment / all | 0 / 0 | 4 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune system disorders | | | |
| Allergic reaction | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 70 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anaphylaxis | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 70 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 70 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 70 (1.43%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nausea | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 2 / 70 (2.86%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vomiting | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 2 / 70 (2.86%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Hyperhidrosis | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 70 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|----------------|----------------|--|
| Nail discolouration | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 70 (1.43%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Palmar-plantar erythrodysesthesia syndrome | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 4 / 70 (5.71%) | |
| occurrences causally related to treatment / all | 0 / 0 | 10 / 10 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Infections | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 70 (1.43%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Anorexia | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 1 / 70 (1.43%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyponatremia | | | |
| subjects affected / exposed | 0 / 63 (0.00%) | 2 / 70 (2.86%) | |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

Frequency threshold for reporting non-serious adverse events: 0 %

| Non-serious adverse events | Analysis Population Paclitaxel | Analysis Population VEX | |
|---|-----------------------------------|----------------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 63 / 63 (100.00%) | 70 / 70 (100.00%) | |
| Vascular disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 1 / 63 (1.59%) | 0 / 70 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| General disorders and administration site conditions | | | |

| | | | |
|---|-------------------------|-------------------------|--|
| Fatigue subjects affected / exposed occurrences (all) | 36 / 63 (57.14%) 131 | 31 / 70 (44.29%) 151 | |
| Injection site reaction subjects affected / exposed occurrences (all) | 2 / 63 (3.17%) 2 | 0 / 70 (0.00%) 0 | |
| Sudden death NOS subjects affected / exposed occurrences (all) | 0 / 63 (0.00%) 0 | 1 / 70 (1.43%) 1 | |
| Immune system disorders Allergic reaction subjects affected / exposed occurrences (all) | 6 / 63 (9.52%) 8 | 2 / 70 (2.86%) 2 | |
| Anaphylaxis subjects affected / exposed occurrences (all) | 1 / 63 (1.59%) 1 | 0 / 70 (0.00%) 0 | |
| Respiratory, thoracic and mediastinal disorders Pleural effusion subjects affected / exposed occurrences (all) | 0 / 63 (0.00%) 0 | 2 / 70 (2.86%) 2 | |
| Pulmonary edema subjects affected / exposed occurrences (all) | 0 / 63 (0.00%) 0 | 1 / 70 (1.43%) 1 | |
| Respiratory, thoracic and mediastinal disorders - Other subjects affected / exposed occurrences (all) | 0 / 63 (0.00%) 0 | 1 / 70 (1.43%) 1 | |
| Investigations Neutrophil count decreased subjects affected / exposed occurrences (all) | 13 / 63 (20.63%) 62 | 11 / 70 (15.71%) 49 | |
| Asparate aminotransferase increased subjects affected / exposed occurrences (all) | 19 / 63 (30.16%) 35 | 14 / 70 (20.00%) 49 | |
| Alkaline phosphatase increased subjects affected / exposed occurrences (all) | 1 / 63 (1.59%) 1 | 0 / 70 (0.00%) 0 | |

| | | | |
|--|---------------------|---------------------|--|
| Blood bilirubin increased subjects affected / exposed occurrences (all) | 0 / 63 (0.00%) 0 | 1 / 70 (1.43%) 1 | |
| GGT increased subjects affected / exposed occurrences (all) | 1 / 63 (1.59%) 1 | 0 / 70 (0.00%) 0 | |
| Injury, poisoning and procedural complications | | | |
| Fracture subjects affected / exposed occurrences (all) | 0 / 63 (0.00%) 0 | 2 / 70 (2.86%) 2 | |
| Hip fracture subjects affected / exposed occurrences (all) | 1 / 63 (1.59%) 1 | 0 / 70 (0.00%) 0 | |
| Cardiac disorders | | | |
| Acute coronary syndrome subjects affected / exposed occurrences (all) | 1 / 63 (1.59%) 1 | 0 / 70 (0.00%) 0 | |
| Aortic valve disease subjects affected / exposed occurrences (all) | 0 / 63 (0.00%) 0 | 1 / 70 (1.43%) 1 | |
| Atrial flutter subjects affected / exposed occurrences (all) | 0 / 63 (0.00%) 0 | 1 / 70 (1.43%) 1 | |
| Supraventricular tachycardia subjects affected / exposed occurrences (all) | 3 / 63 (4.76%) 3 | 4 / 70 (5.71%) 6 | |
| Ventricular arrhythmia subjects affected / exposed occurrences (all) | 1 / 63 (1.59%) 1 | 0 / 70 (0.00%) 0 | |
| Nervous system disorders | | | |
| Depressed level of consciousness subjects affected / exposed occurrences (all) | 0 / 63 (0.00%) 0 | 1 / 70 (1.43%) 1 | |
| Facial nerve disorder subjects affected / exposed occurrences (all) | 0 / 63 (0.00%) 0 | 1 / 70 (1.43%) 1 | |

| | | | |
|---|-------------------------|-------------------------|--|
| Optic nerve disorder subjects affected / exposed occurrences (all) | 1 / 63 (1.59%) 1 | 2 / 70 (2.86%) 2 | |
| Peripheral sensory neuropathy subjects affected / exposed occurrences (all) | 30 / 63 (47.62%) 228 | 5 / 70 (7.14%) 40 | |
| Blood and lymphatic system disorders | | | |
| Anaemia subjects affected / exposed occurrences (all) | 41 / 63 (65.08%) 233 | 26 / 70 (37.14%) 154 | |
| Thrombocytopenia subjects affected / exposed occurrences (all) | 2 / 63 (3.17%) 3 | 10 / 70 (14.29%) 38 | |
| Eye disorders | | | |
| Cataract subjects affected / exposed occurrences (all) | 0 / 63 (0.00%) 0 | 1 / 70 (1.43%) 1 | |
| Gastrointestinal disorders | | | |
| Ascites subjects affected / exposed occurrences (all) | 1 / 63 (1.59%) 1 | 2 / 70 (2.86%) 3 | |
| Constipation subjects affected / exposed occurrences (all) | 13 / 63 (20.63%) 25 | 6 / 70 (8.57%) 13 | |
| Diarrhoea subjects affected / exposed occurrences (all) | 12 / 63 (19.05%) 23 | 22 / 70 (31.43%) 63 | |
| Mucositis oral subjects affected / exposed occurrences (all) | 7 / 63 (11.11%) 14 | 5 / 70 (7.14%) 13 | |
| Nausea subjects affected / exposed occurrences (all) | 17 / 63 (26.98%) 34 | 30 / 70 (42.86%) 154 | |
| Vomiting subjects affected / exposed occurrences (all) | 9 / 63 (14.29%) 9 | 8 / 70 (11.43%) 35 | |
| Skin and subcutaneous tissue disorders | | | |

| | | | | |
|---|-----------------------------|------------------|------------------|--|
| Alopecia | subjects affected / exposed | 21 / 63 (33.33%) | 2 / 70 (2.86%) | |
| | occurrences (all) | 138 | 9 | |
| Palmar-plantar erythrodysesthesia syndrome | subjects affected / exposed | 5 / 63 (7.94%) | 5 / 70 (7.14%) | |
| | occurrences (all) | 23 | 38 | |
| Musculoskeletal and connective tissue disorders | | | | |
| Arthralgia and/or myalgia | subjects affected / exposed | 22 / 63 (34.92%) | 20 / 70 (28.57%) | |
| | occurrences (all) | 75 | 84 | |
| Infections and infestations | | | | |
| Infection | subjects affected / exposed | 20 / 63 (31.75%) | 14 / 70 (20.00%) | |
| | occurrences (all) | 48 | 42 | |
| Metabolism and nutrition disorders | | | | |
| Anorexia | subjects affected / exposed | 1 / 63 (1.59%) | 5 / 70 (7.14%) | |
| | occurrences (all) | 1 | 19 | |
| Hyperglycemia | subjects affected / exposed | 1 / 63 (1.59%) | 0 / 70 (0.00%) | |
| | occurrences (all) | 1 | 0 | |
| Hyponatremia | subjects affected / exposed | 1 / 63 (1.59%) | 1 / 70 (1.43%) | |
| | occurrences (all) | 1 | 1 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported