



Clinical trial results:

A two-arm randomized open label phase 2 study of CP-751,871 in combination with Exemestane versus Exemestane alone as first line treatment for postmenopausal patients with hormone receptor positive advanced breast cancer

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2006-005573-21 |
| Trial protocol | BE NL GB SE IT |
| Global end of trial date | 10 June 2014 |

Results information

| | |
|--------------------------------|--|
| Result version number | v2 (current) |
| This version publication date | 12 March 2016 |
| First version publication date | 02 August 2015 |
| Version creation reason | <ul style="list-style-type: none">• Correction of full data set Reporting periods and duplicate Adverse Events in their data |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | A4021004 |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00372996 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Pfizer Inc. |
| Sponsor organisation address | 235 E 42nd Street, New York, United States, NY 10017 |
| Public contact | Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 001 800-718-1021, ClinicalTrials.govCallCenter@pfizer.com |
| Scientific contact | Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., 001 800-718-1021, ClinicalTrials.govCallCenter@pfizer.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 | 20 May 2015 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|--------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 10 June 2014 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

The main objective of this two arm randomized trial is to compare the efficacy, in terms of progression free survival (PFS), of CP-751,871 in combination with exemestane versus exemestane alone as first line treatment of postmenopausal women with hormone-dependent advanced breast cancer with low risk for the development of diabetes Glycated hemoglobin (Hb A1C) less than (<) 5.7 percent (%).

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 19 February 2007 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety, Efficacy |
| Long term follow-up duration | 5 Months |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Netherlands: 2 |
| Country: Number of subjects enrolled | United Kingdom: 2 |
| Country: Number of subjects enrolled | Belgium: 52 |
| Country: Number of subjects enrolled | Italy: 7 |
| Country: Number of subjects enrolled | Brazil: 47 |
| Country: Number of subjects enrolled | Canada: 28 |
| Country: Number of subjects enrolled | United States: 52 |
| Country: Number of subjects enrolled | Argentina: 29 |
| Worldwide total number of subjects | 219 |
| EEA total number of subjects | 63 |

Notes:

Subjects enrolled per age group

| | |
|--|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 | 0 |

| | |
|--|-----|
| wk | |
| 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) | 130 |
| From 65 to 84 years | 88 |
| 85 years and over | 1 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 219 subjects were enrolled in the study from 8 countries. The study started on 19 February 2007 and ended on 10 June 2014.

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 | CP-751,871 plus (+) Exemestane |

Arm description:

Subjects received CP-751,871 on Day 1 of each 3-week cycle in combination with exemestane once daily, until disease progression.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | Exemestane |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Exemestane was administered at a dose of 25 mg once in a daily.

| | |
|--|-----------------|
| Investigational medicinal product name | CP-751,871 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

CP-751,871 was administered at dose of 20 milligrams per kilogram (mg/Kg).

| | |
|------------------|--|
| Arm title | CP-751,871 + Exemestane/CP-751,871 + Fulvestrant |
|------------------|--|

Arm description:

Subjects received CP-751,871 on day 1 of each 3-week cycle in combination with exemestane once daily, until disease progression. Subjects who experienced disease progression received salvage therapy with CP-751,871 20 mg/kg on Day 1 of each 4-week cycle in combination with fulvestrant, administered according to the local label and standard clinical practice. Subjects continued salvage treatment if safety and clinical benefit were observed for up to a total of 26 cycles or beyond, if there was continued clinical benefit, safety, and tolerability.

| | |
|--|-----------------|
| Arm type | Experimental |
| Investigational medicinal product name | CP-751,871 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

CP-751,871 was administered at dose of 20 mg/Kg.

| | |
|--|--|
| Investigational medicinal product name | Exemestane |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| Exemestane was administered at a dose of 25 mg once in a day. | |
| Investigational medicinal product name | Fulvestrant |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection in pre-filled syringe |
| Routes of administration | Intramuscular use |
| Dosage and administration details: | |
| Fulvestrant was administered at a dose of 50 mg/ml. | |
| Arm title | Exemestane |
| Arm description: | |
| Subjects received exemestane once daily, until disease progression. | |
| Arm type | Active comparator |
| Investigational medicinal product name | Exemestane |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| Exemestane was administered at a dose of 25 mg once in a day. | |
| Arm title | Exemestane/CP-751,871 + Exemestane |
| Arm description: | |
| Subjects received exemestane once daily, until disease progression. Subjects who experienced disease progression received salvage therapy with CP-751,871 20 mg/kg on Day 1 of each 3-week cycle in combination with exemestane for up to a total of 20 months or beyond if safety and clinical benefit were observed. | |
| Arm type | Active comparator |
| Investigational medicinal product name | Exemestane |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| Exemestane was administered at a dose of 25 mg once in a day. | |
| Investigational medicinal product name | CP-751,871 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |
| Dosage and administration details: | |
| CP-751,871 was administered at dose of 20 mg/Kg. | |

| Number of subjects in period 1 | CP-751,871 plus (+) Exemestane | CP-751,871 + Exemestane/CP- 751,871 + Fulvestrant | Exemestane |
|--------------------------------|-----------------------------------|--|------------|
| | | | |
| Started | 79 | 36 | 61 |
| Completed | 42 | 22 | 33 |
| Not completed | 37 | 14 | 28 |
| Death | 11 | 4 | 8 |
| Not specified | 10 | 2 | 7 |
| Study terminated by sponsor | 4 | - | 4 |
| Lost to follow-up | - | 2 | - |
| Withdrawal by subject | 12 | 6 | 9 |

| Number of subjects in period 1 | Exemestane/CP- 751,871 + Exemestane |
|--------------------------------|---|
| Started | 43 |
| Completed | 23 |
| Not completed | 20 |
| Death | 7 |
| Not specified | 7 |
| Study terminated by sponsor | - |
| Lost to follow-up | 1 |
| Withdrawal by subject | 5 |

Baseline characteristics

Reporting groups

| | |
|--------------------------------|---------------|
| Reporting group title | Overall Study |
| Reporting group description: - | |

| Reporting group values | Overall Study | Total | |
|------------------------|---------------|-------|--|
| Number of subjects | 219 | 219 | |
| Age categorical | | | |
| Units: Subjects | | | |

| | | | |
|--------------------|---------|-----|--|
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 61.9 | | |
| standard deviation | ± 10.82 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 219 | 219 | |
| Male | 0 | 0 | |

Subject analysis sets

| | |
|----------------------------|-------------------------|
| Subject analysis set title | CP-751,871 + Exemestane |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

Subjects received CP-751,871 20 mg/kg on Day 1 of each 3-week cycle as an IV infusion in combination with exemestane 25 mg tablets, by mouth, once daily, until disease progression. Participants who experienced disease progression could have received salvage therapy with CP-751,871 20 mg/kg on Day 1 of each 4-week cycle in combination with fulvestrant, administered according to the local label and standard clinical practice. Participants continued salvage treatment if safety and clinical benefit were observed for up to a total of 26 cycles or beyond, if there was continued clinical benefit, safety, and tolerability.

| | |
|----------------------------|-----------------|
| Subject analysis set title | Exemestane |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

Subjects received exemestane 25 mg tablets, by mouth, once daily, until disease progression. Participants who experienced disease progression could have received salvage therapy with CP-751,871 20 mg/kg on Day 1 of each 3-week cycle in combination with exemestane 25 mg tablets, by mouth, once daily, for up to a total of 20 months or beyond if safety and clinical benefit were observed.

| Reporting group values | CP-751,871 + Exemestane | Exemestane | |
|------------------------|-------------------------|------------|--|
| Number of subjects | 115 | 104 | |
| Age categorical | | | |
| Units: Subjects | | | |

| | | | |
|--------------------|---------|---------|--|
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 61.2 | 62.7 | |
| standard deviation | ± 10.77 | ± 10.86 | |

| | | | |
|--------------------|-----|-----|--|
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 115 | 104 | |
| Male | 0 | 0 | |

End points

End points reporting groups

| | |
|---|--|
| Reporting group title | CP-751,871 plus (+) Exemestane |
| Reporting group description: Subjects received CP-751,871 on Day 1 of each 3-week cycle in combination with exemestane once daily, until disease progression. | |
| Reporting group title | CP-751,871 + Exemestane/CP-751,871 + Fulvestrant |
| Reporting group description: Subjects received CP-751,871 on day 1 of each 3-week cycle in combination with exemestane once daily, until disease progression. Subjects who experienced disease progression received salvage therapy with CP-751,871 20 mg/kg on Day 1 of each 4-week cycle in combination with fulvestrant, administered according to the local label and standard clinical practice. Subjects continued salvage treatment if safety and clinical benefit were observed for up to a total of 26 cycles or beyond, if there was continued clinical benefit, safety, and tolerability. | |
| Reporting group title | Exemestane |
| Reporting group description: Subjects received exemestane once daily, until disease progression. | |
| Reporting group title | Exemestane/CP-751,871 + Exemestane |
| Reporting group description: Subjects received exemestane once daily, until disease progression. Subjects who experienced disease progression received salvage therapy with CP-751,871 20 mg/kg on Day 1 of each 3-week cycle in combination with exemestane for up to a total of 20 months or beyond if safety and clinical benefit were observed. | |
| Subject analysis set title | CP-751,871 + Exemestane |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: Subjects received CP-751,871 20 mg/kg on Day 1 of each 3-week cycle as an IV infusion in combination with exemestane 25 mg tablets, by mouth, once daily, until disease progression. Participants who experienced disease progression could have received salvage therapy with CP-751,871 20 mg/kg on Day 1 of each 4-week cycle in combination with fulvestrant, administered according to the local label and standard clinical practice. Participants continued salvage treatment if safety and clinical benefit were observed for up to a total of 26 cycles or beyond, if there was continued clinical benefit, safety, and tolerability. | |
| Subject analysis set title | Exemestane |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: Subjects received exemestane 25 mg tablets, by mouth, once daily, until disease progression. Participants who experienced disease progression could have received salvage therapy with CP-751,871 20 mg/kg on Day 1 of each 3-week cycle in combination with exemestane 25 mg tablets, by mouth, once daily, for up to a total of 20 months or beyond if safety and clinical benefit were observed. | |

Primary: Primary: Progression-Free Survival (PFS)

| | |
|--|--|
| End point title | Primary: Progression-Free Survival (PFS) |
| End point description: PFS was calculated from time of randomization to progression of disease, death or treatment discontinuation because of unsatisfactory results. Disease progression: radiographic progression (20 percent [%] increase in measurable lesions, appearance of new lesions or unequivocal progression of evaluable lesions as defined by Response Evaluation Criteria in Solid Tumors [RECIST]); occurrence of new pleural/pericardial effusions or ascites confirmed by positive cytology; persistent hypercalcemia requiring more than 2 IV treatments with bisphosphonates; intervention for any cancer-related events or symptoms related to tumor growth requiring subject discontinuation, development of brain metastasis or death. Median PFS was estimated from Kaplan-Meier curve. 95% confidence interval (CI) is based on Brookmeyer and Crowley method. Full Analysis Set (FAS): all enrolled subjects; grouped by randomized arm, where first 10 subjects enrolled but not randomly assigned to treatment were not included. | |
| End point type | Primary |

End point timeframe:

Baseline, Day 1 of Cycles 2 and 4 and then Day 1 of every 3rd cycle starting at Cycle 7 up to 60 months.

| End point values | CP-751,871 + Exemestane | Exemestane | | |
|----------------------------------|-------------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 106 | 103 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 11 (8.1 to 12.9) | 9.2 (7 to 13) | | |

Statistical analyses

| Statistical analysis title | Exemestane, CP-751,871 + Exemestane |
|--|--------------------------------------|
| Statistical analysis description: 2-sided p-value from an unstratified log-rank test. Hazard ratio was based on Cox proportional hazards model. | |
| Comparison groups | CP-751,871 + Exemestane v Exemestane |
| Number of subjects included in analysis | 209 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.56 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.912 |
| Confidence interval | |
| level | Other: 80 % |
| sides | 2-sided |
| lower limit | 0.744 |
| upper limit | 1.118 |

Primary: PFS in Subjects with Hemoglobin A1c (HbA1c) Less than (<) 5.7% at Baseline

| | |
|---|--|
| End point title | PFS in Subjects with Hemoglobin A1c (HbA1c) Less than (<) 5.7% at Baseline |
| End point description: PFS was calculated from the time of randomization to either progression of disease, death, or treatment discontinuation because of unsatisfactory therapy results (such as global deterioration of health status). Disease progression was defined as 1 or more of the following: radiographic progression (20% increase in measurable lesions, appearance of new lesions or unequivocal progression of evaluable lesions as defined by RECIST); occurrence of new pleural/pericardial effusions or ascites confirmed by positive cytology; persistent hypercalcemia requiring more than 2 IV treatments with bisphosphonates; intervention for any cancer-related events (radiations, surgery) or new symptoms related to tumor growth requiring subject discontinuation; development of brain metastasis; or death for any cause. Median PFS was estimated from the Kaplan-Meier curve. 95% CI is based on the Brookmeyer and Crowley method. FAS; only subjects with baseline HbA1c <5.7% were included in the analysis. | |
| End point type | Primary |

End point timeframe:

Baseline, Day 1 of Cycles 2 and 4 and then Day 1 of every 3rd cycle starting at Cycle 7 up to 60 months

| End point values | CP-751,871 + Exemestane | Exemestane | | |
|----------------------------------|-------------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 39 | 40 | | |
| Units: months | | | | |
| median (confidence interval 95%) | 13.2 (8.1 to 19.5) | 9.9 (7 to 13.6) | | |

Statistical analyses

| Statistical analysis title | Exemestane, CP-751,871 + Exemestane |
|---|--------------------------------------|
| Statistical analysis description: 2-sided p-value from unstratified log-rank test. Hazard ratio was based on the Cox proportional hazards model. | |
| Comparison groups | Exemestane v CP-751,871 + Exemestane |
| Number of subjects included in analysis | 79 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.331 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.764 |
| Confidence interval | |
| level | Other: 70 % |
| sides | 2-sided |
| lower limit | 0.572 |
| upper limit | 1.02 |

Secondary: Percentage of Subjects Achieving Complete Response (CR), Partial Response (PR), or Stable Disease (SD) Maintained for at Least 6 Months

| | |
|--|---|
| End point title | Percentage of Subjects Achieving Complete Response (CR), Partial Response (PR), or Stable Disease (SD) Maintained for at Least 6 Months |
| End point description: Objective responses were defined using RECIST as CR: disappearance of all target and non target lesions. PR: at least a 30% decrease in the sum of the longest diameter (LD) of target lesions, taking as a reference the baseline sum LD. Non target lesions may persist provided there is no unequivocal progression in these lesions. SD: measurements demonstrating neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify as progressive disease (PD) during the first 6 weeks after the start of treatment taking as reference the smallest sum LD since the treatment started. During this time, non target lesions may persist provided there is no unequivocal progression in these lesions. FAS: : all enrolled subjects; grouped by randomized arm, where first 10 subjects enrolled but not randomly assigned to treatment were not included. | |
| End point type | Secondary |

End point timeframe:

Baseline, Day 1 of Cycles 2 and 4 and then Day 1 of every 3rd cycle starting at Cycle 7 up to 60 months

| End point values | CP-751,871 + Exemestane | Exemestane | | |
|----------------------------------|-------------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 106 | 103 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | 68.9 (59.1 to 77.5) | 64.1 (54 to 73.3) | | |

Statistical analyses

| Statistical analysis title | CP-751,871 + Exemestane, Exemestane |
|---|--------------------------------------|
| Comparison groups | CP-751,871 + Exemestane v Exemestane |
| Number of subjects included in analysis | 209 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.463 |
| Method | Pearson chi-square test |
| Parameter estimate | Mean difference (net) |
| Point estimate | 4.79 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -8 |
| upper limit | 17.6 |

Secondary: Maximum Plasma Concentration of CP-751,871

| | |
|------------------------|--|
| End point title | Maximum Plasma Concentration of CP-751,871 |
| End point description: | The analysis population included all subjects treated with CP-751,871. However, the study was terminated early due to strategic reasons and pharmacokinetic (PK) sampling was discontinued by Protocol Amendment 6. Therefore, the analysis was not performed. Data from samples that were collected and analyzed were listed descriptively. |
| End point type | Secondary |
| End point timeframe: | Predose on Day 1 at Cycles 1, 2, 4, and 5 and 150 days post last dose of CP-751,871 and for salvage therapy, at Day 1 and 150 days post last dose of CP-751,871 |

| | | | | |
|--|-------------------------|--|--|--|
| End point values | CP-751,871 + Exemestane | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 0 ^[1] | | | |
| Units: ng/mL (nanogram per milliliter) | | | | |
| arithmetic mean (standard deviation) | () | | | |

Notes:

[1] - Although some samples were collected, analysis was not performed due to study termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Minimum Plasma Concentration of CP-751,871

| | |
|-----------------|--|
| End point title | Minimum Plasma Concentration of CP-751,871 |
|-----------------|--|

End point description:

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

End point timeframe:

Predose on Day 1 at Cycles 1, 2, 4, and 5 and 150 days post last dose of CP-751,871 and for salvage therapy, at Day 1 and 150 days post last dose of CP-751,871

| | | | | |
|--------------------------------------|-------------------------|--|--|--|
| End point values | CP-751,871 + Exemestane | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 0 ^[2] | | | |
| Units: ng/mL | | | | |
| arithmetic mean (standard deviation) | () | | | |

Notes:

[2] - Although some samples were collected, analysis was not performed due to study termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Concentration Time Curve from Time 0 to the Last Time Point with Quantifiable Concentration

| | |
|-----------------|--|
| End point title | Area Under the Concentration Time Curve from Time 0 to the Last Time Point with Quantifiable Concentration |
|-----------------|--|

End point description:

The analysis population included all subjects treated with CP-751,871. However, the study was terminated early due to strategic reasons and PK sampling was discontinued by Protocol Amendment 6. Therefore, the analysis was not performed. Data from samples that were collected and analyzed were listed descriptively.

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

End point timeframe:

Predose on Day 1 at Cycles 1, 2, 4, and 5 and 150 days post last dose of CP-751,871 and for salvage therapy, at Day 1 and 150 days post last dose of CP-751,871

| | | | | |
|--|-------------------------|--|--|--|
| End point values | CP-751,871 + Exemestane | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 0 ^[3] | | | |
| Units: ng*h/mL (naonogram*hour/milliliter) | | | | |
| arithmetic mean (standard deviation) | () | | | |

Notes:

[3] - Although some samples were collected, analysis was not performed due to study termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Negative Human Anti-Human Antibodies (HAHAs)

| | |
|-----------------|--|
| End point title | Number of Subjects with Negative Human Anti-Human Antibodies (HAHAs) |
|-----------------|--|

End point description:

Negative human anti-human antibodies were defined as <6.64. All randomized subjects who started treatment and who had at least 1 sample submitted for the biomarker; collection of samples for this analysis was stopped after Amendment 6. All samples were negative to HAHA.

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

End point timeframe:

Predose on Day 1 of Cycle 1 and at 150 days post last CP-751,871 infusion

| | | | | |
|------------------------------|-------------------------|--|--|--|
| End point values | CP-751,871 + Exemestane | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 37 | | | |
| Units: subjects | | | | |
| Number of Subjects Analyzed: | 37 | | | |
| Number of Samples Analyzed | 66 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with Circulating Tumor Cells Expressing Insulin-Like Growth Factor 1 Receptor (IGF-IR)

| | |
|-----------------|---|
| End point title | Percentage of subjects with Circulating Tumor Cells Expressing Insulin-Like Growth Factor 1 Receptor (IGF-IR) |
|-----------------|---|

End point description:

The analysis population included all subjects treated with CP-751,871. However, the study was terminated early due to strategic reasons and biomarker sampling was discontinued by Protocol

Amendment 6. Therefore, the analysis was not performed. Data from samples that were collected and analyzed were listed descriptively.

| | |
|-----------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Predose on Day 1 of Cycle 1 | |

| End point values | CP-751,871 + Exemestane | Exemestane | | |
|-------------------------------|-------------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 0 ^[4] | 0 ^[5] | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |

Notes:

[4] - Although some samples were collected, analysis was not performed due to study termination.

[5] - Although some samples were collected, analysis was not performed due to study termination.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Serum Markers Relevant to the IGF-1R Pathway

| | |
|-----------------|--|
| End point title | Percentage of Subjects with Serum Markers Relevant to the IGF-1R Pathway |
|-----------------|--|

End point description:

The analysis population included all subjects treated with CP-751,871. However, the study was terminated early due to strategic reasons and biomarker sampling was discontinued by Protocol Amendment 6. Therefore, the analysis was not performed.

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

End point timeframe:

Predose on Day 1 of Cycles 1 and 4 and at end of treatment prior to beginning salvage therapy

| End point values | CP-751,871 + Exemestane | Exemestane | | |
|-----------------------------|-------------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 0 ^[6] | 0 ^[7] | | |
| Units: subjects | | | | |

Notes:

[6] - Although some samples were collected, analysis was not performed due to study termination.

[7] - Although some samples were collected, analysis was not performed due to study termination.

Statistical analyses

No statistical analyses for this end point

Secondary: European Organization for the Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire 30 (QLQ-C30) Scores

| | |
|-----------------|---|
| End point title | European Organization for the Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire 30 (QLQ-C30) |
|-----------------|---|

End point description:

EORTC QLQ-C30: included functional scales (physical, role, cognitive, emotional, and social), global health status, symptom scales (fatigue, pain, nausea/vomiting) and single items (dyspnoea, appetite loss, insomnia, constipation/diarrhea and financial difficulties). Most questions used 4 point scale (1 'Not at all' to 4 'Very much'; 2 questions used 7-point scale (1 'very poor' to 7 'Excellent'). Scores averaged, transformed to 0-100 scale; higher score equals (=) better level of functioning or greater degree of symptoms. The study was terminated early secondary to strategic reasons and the questionnaires were discontinued by Protocol Amendment 6. Data already collected were not analyzed`.

End point type Secondary

End point timeframe:

Predose on Day 1 of each cycle, at the end of treatment and at follow-up, up to 60 months

| End point values | CP-751,871 + Exemestane | Exemestane | | |
|--------------------------------------|-------------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 0 ^[8] | 0 ^[9] | | |
| Units: scores on a scale | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[8] - Although some questionnaires were collected, analysis was not done due to termination of the study

[9] - Although some questionnaires were collected, analysis was not done due to termination of the study

Statistical analyses

No statistical analyses for this end point

Secondary: EORTC QLQ Breast Cancer Module (BR23) Scores

End point title EORTC QLQ Breast Cancer Module (BR23) Scores

End point description:

EORTC-QLQ-BR23: included functional scales (body image, sexual functioning, sexual enjoyment, and future perspective) and single item symptoms scales (systemic therapy side effects, breast symptoms, arm symptoms, and upset by hair loss). Questions used 4-point Likert scale (1 'Not at All' to 4 'Very Much'). Scores averaged and transformed to 0-100 scale. High score for functional scale=high/healthy level of functioning. High score for single item=high level of symptomatology/problems. Change from baseline=Cycle/Day score minus baseline score. The study was terminated early secondary to strategic reasons and the questionnaires were discontinued by Protocol Amendment 6. Data already collected were not analyzed.

End point type Secondary

End point timeframe:

Predose on Day 1, at end of treatment, and at Follow-up, up to 60 months

| End point values | CP-751,871 + Exemestane | Exemestane | | |
|--------------------------------------|-------------------------|----------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 0 ^[10] | 0 ^[11] | | |
| Units: scores on a scale | | | | |
| arithmetic mean (standard deviation) | () | () | | |

Notes:

[10] - Although some samples were collected, analysis was not performed due to study termination.

[11] - Although some samples were collected, analysis was not performed due to study termination.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events (AEs) recorded from informed consent through and including 150 calendar days after the last administration of investigational product. Active reporting period for exemestane/fulvestrant clarified to 28 days after last dose in Amendment 6.

Adverse event reporting additional description:

The same event may appear as both an AE and a serious AE (SAE). However, what is presented are distinct events. An event may be categorized as serious in 1 subject and as nonserious in another subject, or 1 subject may have experienced both a serious and nonserious event during the study.

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 17.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-------------------------|
| Reporting group title | CP-751,871 + Exemestane |
|-----------------------|-------------------------|

Reporting group description:

Subjects received CP-751,871 20 mg/kg on Day 1 of each 3-week cycle as an IV infusion in combination with exemestane 25 mg tablets, by mouth, once daily, until disease progression.

| | |
|-----------------------|--|
| Reporting group title | CP-751,871 + Fulvestrant (after CP-751,871+Exemestane) |
|-----------------------|--|

Reporting group description:

Subjects received CP-751,871 20 mg/kg on Day 1 of each 3-week cycle as an IV infusion in combination with exemestane 25 mg tablets, by mouth, once daily, until disease progression. Subjects who experienced disease progression received salvage therapy with CP-751,871 20 mg/kg on Day 1 of each 4-week cycle in combination with fulvestrant, administered according to the local label and standard clinical practice. Subjects continued salvage treatment if safety and clinical benefit were observed for up to a total of 26 cycles or beyond, if there was continued clinical benefit, safety, and tolerability. Adverse events are presented from the period of time when the subject was receiving salvage therapy treatment only.

| | |
|-----------------------|------------|
| Reporting group title | Exemestane |
|-----------------------|------------|

Reporting group description:

Subjects received exemestane 25 mg tablets, by mouth, once daily, until disease progression.

| | |
|-----------------------|--|
| Reporting group title | CP-751,871 + Exemestane (after Exemestane) |
|-----------------------|--|

Reporting group description:

Subjects received exemestane 25 mg tablets, by mouth, once daily, until disease progression. Subjects who experienced disease progression received salvage therapy with CP-751,871 20 mg/kg on Day 1 of each 3-week cycle in combination with exemestane 25 mg tablets, by mouth, once daily, for up to a total of 20 months or beyond if safety and clinical benefit were observed. Adverse events are presented from the period of time when the subject was receiving salvage therapy treatment only.

| Serious adverse events | CP-751,871 + Exemestane | CP-751,871 + Fulvestrant (after CP-751,871+Exemestane) | Exemestane |
|---|-------------------------|--|-------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 38 / 115 (33.04%) | 11 / 36 (30.56%) | 23 / 104 (22.12%) |
| number of deaths (all causes) | 11 | 3 | 8 |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| Breast cancer | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 6 | 0 / 2 | 0 / 5 |
| Pancreatic carcinoma | | | |
| subjects affected / exposed | 0 / 115 (0.00%) | 0 / 36 (0.00%) | 1 / 104 (0.96%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Lung neoplasm malignant | | | |
| subjects affected / exposed | 0 / 115 (0.00%) | 0 / 36 (0.00%) | 1 / 104 (0.96%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lymphangiosis carcinomatosa | | | |
| subjects affected / exposed | 0 / 115 (0.00%) | 0 / 36 (0.00%) | 1 / 104 (0.96%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Malignant neoplasm progression | | | |
| subjects affected / exposed | 0 / 115 (0.00%) | 0 / 36 (0.00%) | 2 / 104 (1.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal cord neoplasm | | | |
| subjects affected / exposed | 0 / 115 (0.00%) | 1 / 36 (2.78%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vulval cancer | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Haemorrhage | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Deep vein thrombosis | | | |

| | | | |
|--|-----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 115 (0.00%) | 0 / 36 (0.00%) | 1 / 104 (0.96%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Embolism | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypertension | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Venous insufficiency | | | |
| subjects affected / exposed | 0 / 115 (0.00%) | 1 / 36 (2.78%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Surgical and medical procedures | | | |
| Open reduction of fracture | | | |
| subjects affected / exposed | 0 / 115 (0.00%) | 0 / 36 (0.00%) | 1 / 104 (0.96%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Disease progression | | | |
| subjects affected / exposed | 5 / 115 (4.35%) | 2 / 36 (5.56%) | 4 / 104 (3.85%) |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 2 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 6 | 0 / 2 | 0 / 7 |
| Asthenia | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | 0 / 36 (0.00%) | 1 / 104 (0.96%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chest pain | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | 0 / 36 (0.00%) | 1 / 104 (0.96%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|----------------|-----------------|
| General physical health deterioration | | | |
| subjects affected / exposed | 0 / 115 (0.00%) | 1 / 36 (2.78%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Impaired healing | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Malaise | | | |
| subjects affected / exposed | 2 / 115 (1.74%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mucosal inflammation | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | 0 / 36 (0.00%) | 1 / 104 (0.96%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pain | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 115 (0.00%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |
| Hypersensitivity | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Respiratory failure | | | |
| subjects affected / exposed | 0 / 115 (0.00%) | 1 / 36 (2.78%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |

| | | | |
|---|-----------------|----------------|-----------------|
| Apnoea | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 115 (0.00%) | 0 / 36 (0.00%) | 1 / 104 (0.96%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Epistaxis | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemoptysis | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemothorax | | | |
| subjects affected / exposed | 0 / 115 (0.00%) | 0 / 36 (0.00%) | 1 / 104 (0.96%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Organising pneumonia | | | |
| subjects affected / exposed | 0 / 115 (0.00%) | 0 / 36 (0.00%) | 1 / 104 (0.96%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary embolism | | | |
| subjects affected / exposed | 0 / 115 (0.00%) | 1 / 36 (2.78%) | 2 / 104 (1.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Confusional state | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Insomnia | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 115 (0.00%) | 0 / 36 (0.00%) | 1 / 104 (0.96%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Suicidal ideation | | | |
| subjects affected / exposed | 0 / 115 (0.00%) | 0 / 36 (0.00%) | 1 / 104 (0.96%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Subdural haematoma | | | |
| subjects affected / exposed | 2 / 115 (1.74%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Craniocerebral injury | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fall | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Femur fracture | | | |
| subjects affected / exposed | 0 / 115 (0.00%) | 1 / 36 (2.78%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hip fracture | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Humerus fracture | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | 1 / 36 (2.78%) | 0 / 104 (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 |
| Radius fracture | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed | 1 / 115 (0.87%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Scapula fracture | | | |
| subjects affected / exposed | 0 / 115 (0.00%) | 1 / 36 (2.78%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal compression fracture | | | |
| subjects affected / exposed | 0 / 115 (0.00%) | 1 / 36 (2.78%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper limb fracture | | | |
| subjects affected / exposed | 0 / 115 (0.00%) | 0 / 36 (0.00%) | 1 / 104 (0.96%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Cardiac failure | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Aphasia | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Balance disorder | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebral haemorrhage | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebral ischaemia | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 115 (0.00%) | 1 / 36 (2.78%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 0 / 115 (0.00%) | 1 / 36 (2.78%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Depressed level of consciousness | | | |
| subjects affected / exposed | 0 / 115 (0.00%) | 0 / 36 (0.00%) | 1 / 104 (0.96%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dysarthria | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Grand mal convulsion | | | |
| subjects affected / exposed | 2 / 115 (1.74%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Headache | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peripheral sensory neuropathy | | | |
| subjects affected / exposed | 0 / 115 (0.00%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sensory loss | | | |
| subjects affected / exposed | 2 / 115 (1.74%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Syncope | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed | 1 / 115 (0.87%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 2 / 115 (1.74%) | 0 / 36 (0.00%) | 2 / 104 (1.92%) |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neutropenia | | | |
| subjects affected / exposed | 0 / 115 (0.00%) | 0 / 36 (0.00%) | 1 / 104 (0.96%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancytopenia | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | 0 / 36 (0.00%) | 1 / 104 (0.96%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Eye disorders | | | |
| Cataract | | | |
| subjects affected / exposed | 0 / 115 (0.00%) | 1 / 36 (2.78%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Macular fibrosis | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | 1 / 36 (2.78%) | 0 / 104 (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 |
| Gastrointestinal disorders | | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 0 / 115 (0.00%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|----------------|-----------------|
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | 1 / 36 (2.78%) | 1 / 104 (0.96%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal rigidity | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Constipation | | | |
| subjects affected / exposed | 0 / 115 (0.00%) | 0 / 36 (0.00%) | 1 / 104 (0.96%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 115 (0.00%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dysphagia | | | |
| subjects affected / exposed | 0 / 115 (0.00%) | 0 / 36 (0.00%) | 1 / 104 (0.96%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastric ulcer | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal toxicity | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 115 (0.00%) | 0 / 36 (0.00%) | 1 / 104 (0.96%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nausea | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed | 1 / 115 (0.87%) | 0 / 36 (0.00%) | 1 / 104 (0.96%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatitis acute | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Stomatitis | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vomiting | | | |
| subjects affected / exposed | 3 / 115 (2.61%) | 0 / 36 (0.00%) | 1 / 104 (0.96%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Portal vein thrombosis | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| Cholelithiasis | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Skin mass | | | |
| subjects affected / exposed | 0 / 115 (0.00%) | 0 / 36 (0.00%) | 1 / 104 (0.96%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Haematuria | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|----------------|-----------------|
| Renal failure | | | |
| subjects affected / exposed | 0 / 115 (0.00%) | 0 / 36 (0.00%) | 1 / 104 (0.96%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal failure acute | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endocrine disorders | | | |
| Hyperthyroidism | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Bacteraemia | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Bronchopneumonia | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | 0 / 36 (0.00%) | 1 / 104 (0.96%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Pulmonary sepsis | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed | 1 / 115 (0.87%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Sepsis | | | |
| subjects affected / exposed | 0 / 115 (0.00%) | 0 / 36 (0.00%) | 3 / 104 (2.88%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Clostridium difficile colitis | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cystitis | | | |
| subjects affected / exposed | 2 / 115 (1.74%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Erysipelas | | | |
| subjects affected / exposed | 0 / 115 (0.00%) | 0 / 36 (0.00%) | 1 / 104 (0.96%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal infection | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lymphangitis | | | |
| subjects affected / exposed | 0 / 115 (0.00%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peritonitis bacterial | | | |
| subjects affected / exposed | 0 / 115 (0.00%) | 0 / 36 (0.00%) | 1 / 104 (0.96%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 115 (0.00%) | 0 / 36 (0.00%) | 1 / 104 (0.96%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory tract infection | | | |
| subjects affected / exposed | 2 / 115 (1.74%) | 1 / 36 (2.78%) | 0 / 104 (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 |
| Urinary tract infection | | | |
| subjects affected / exposed | 2 / 115 (1.74%) | 0 / 36 (0.00%) | 2 / 104 (1.92%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Viral infection | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | 0 / 36 (0.00%) | 1 / 104 (0.96%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dehydration | | | |
| subjects affected / exposed | 0 / 115 (0.00%) | 1 / 36 (2.78%) | 2 / 104 (1.92%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetes mellitus | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetic ketoacidosis | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypercalcaemia | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed | 1 / 115 (0.87%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyperglycaemia | | | |
| subjects affected / exposed | 8 / 115 (6.96%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences causally related to treatment / all | 8 / 10 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | CP-751,871 + Exemestane (after Exemestane) | | |
|---|--|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 15 / 43 (34.88%) | | |
| number of deaths (all causes) | 6 | | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Breast cancer | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 6 | | |
| Pancreatic carcinoma | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lung neoplasm malignant | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lymphangiosis carcinomatosa | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Malignant neoplasm progression | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Spinal cord neoplasm | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vulval cancer | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| Haemorrhage | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Embolism | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypertension | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Venous insufficiency | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Surgical and medical procedures | | | |

| | | | |
|---|-----------------|--|--|
| Open reduction of fracture subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Disease progression | | | |
| subjects affected / exposed | 6 / 43 (13.95%) | | |
| occurrences causally related to treatment / all | 0 / 7 | | |
| deaths causally related to treatment / all | 0 / 6 | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Chest pain | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General physical health deterioration | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Impaired healing | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Malaise | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Mucosal inflammation | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|----------------|--|--|
| Pain | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Immune system disorders | | | |
| Hypersensitivity | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Respiratory failure | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Apnoea | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Haemoptysis | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|----------------|--|--|
| Haemothorax | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Organising pneumonia | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pulmonary embolism | | | |
| subjects affected / exposed | 2 / 43 (4.65%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychiatric disorders | | | |
| Confusional state | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Insomnia | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Suicidal ideation | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| Subdural haematoma | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Craniocerebral injury | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | | |
|---|----------------|--|--|--|
| Fall | | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Femur fracture | | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hip fracture | | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Humerus fracture | | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Radius fracture | | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Scapula fracture | | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Spinal compression fracture | | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Upper limb fracture | | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cardiac disorders | | | | |

| | | | |
|---|----------------|--|--|
| Cardiac failure | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Aphasia | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Balance disorder | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cerebral haemorrhage | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cerebral ischaemia | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Depressed level of consciousness | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dysarthria | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Grand mal convulsion | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Headache | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Peripheral sensory neuropathy | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sensory loss | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Syncope | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Neutropenia | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pancytopenia | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Thrombocytopenia | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Eye disorders | | | |
| Cataract | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Macular fibrosis | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Abdominal pain | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Abdominal rigidity | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Constipation | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 2 / 43 (4.65%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dysphagia | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastric ulcer | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal toxicity | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nausea | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pancreatitis acute | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Stomatitis | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vomiting | | | |
| subjects affected / exposed | 2 / 43 (4.65%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatobiliary disorders | | | |
| Portal vein thrombosis | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin and subcutaneous tissue disorders | | | |
| Skin mass | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| Haematuria | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal failure | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal failure acute | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Endocrine disorders | | | |
| Hyperthyroidism | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Back pain | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Bacteraemia | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bronchopneumonia | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pulmonary sepsis | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sepsis | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Clostridium difficile colitis | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cystitis | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Erysipelas | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal infection | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lymphangitis | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Peritonitis bacterial | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory tract infection | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Viral infection | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dehydration | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Diabetes mellitus | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Diabetic ketoacidosis | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypercalcaemia | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 2 / 43 (4.65%) | | |
| occurrences causally related to treatment / all | 2 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | CP-751,871 + Exemestane | CP-751,871 + Fulvestrant (after CP-751,871+Exemestane) | Exemestane |
|---|-------------------------|--|-------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 113 / 115 (98.26%) | 34 / 36 (94.44%) | 96 / 104 (92.31%) |
| Vascular disorders | | | |
| Hot flush | | | |
| subjects affected / exposed | 13 / 115 (11.30%) | 5 / 36 (13.89%) | 25 / 104 (24.04%) |
| occurrences (all) | 18 | 7 | 35 |

| | | | |
|--|-------------------------|------------------------|-------------------------|
| Hypertension subjects affected / exposed occurrences (all) | 14 / 115 (12.17%) 17 | 3 / 36 (8.33%) 6 | 4 / 104 (3.85%) 6 |
| General disorders and administration site conditions | | | |
| Asthenia subjects affected / exposed occurrences (all) | 17 / 115 (14.78%) 28 | 3 / 36 (8.33%) 5 | 13 / 104 (12.50%) 18 |
| Chest pain subjects affected / exposed occurrences (all) | 8 / 115 (6.96%) 11 | 2 / 36 (5.56%) 3 | 8 / 104 (7.69%) 10 |
| Fatigue subjects affected / exposed occurrences (all) | 35 / 115 (30.43%) 66 | 11 / 36 (30.56%) 17 | 33 / 104 (31.73%) 57 |
| Influenza like illness subjects affected / exposed occurrences (all) | 6 / 115 (5.22%) 7 | 1 / 36 (2.78%) 1 | 2 / 104 (1.92%) 2 |
| Injection site pain subjects affected / exposed occurrences (all) | 0 / 115 (0.00%) 0 | 2 / 36 (5.56%) 2 | 0 / 104 (0.00%) 0 |
| Oedema peripheral subjects affected / exposed occurrences (all) | 5 / 115 (4.35%) 7 | 1 / 36 (2.78%) 2 | 10 / 104 (9.62%) 19 |
| Pain subjects affected / exposed occurrences (all) | 7 / 115 (6.09%) 10 | 2 / 36 (5.56%) 2 | 8 / 104 (7.69%) 10 |
| Pyrexia subjects affected / exposed occurrences (all) | 11 / 115 (9.57%) 13 | 1 / 36 (2.78%) 1 | 5 / 104 (4.81%) 5 |
| Reproductive system and breast disorders | | | |
| Breast pain subjects affected / exposed occurrences (all) | 6 / 115 (5.22%) 8 | 2 / 36 (5.56%) 5 | 10 / 104 (9.62%) 15 |
| Pelvic pain subjects affected / exposed occurrences (all) | 4 / 115 (3.48%) 5 | 2 / 36 (5.56%) 2 | 3 / 104 (2.88%) 4 |
| Vulvovaginal dryness | | | |

| | | | |
|--|----------------------|---------------------|----------------------|
| subjects affected / exposed occurrences (all) | 6 / 115 (5.22%) 6 | 3 / 36 (8.33%) 4 | 3 / 104 (2.88%) 3 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 23 / 115 (20.00%) | 4 / 36 (11.11%) | 17 / 104 (16.35%) |
| occurrences (all) | 33 | 6 | 26 |
| Dyspnoea | | | |
| subjects affected / exposed | 19 / 115 (16.52%) | 6 / 36 (16.67%) | 14 / 104 (13.46%) |
| occurrences (all) | 29 | 9 | 22 |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 7 / 115 (6.09%) | 0 / 36 (0.00%) | 2 / 104 (1.92%) |
| occurrences (all) | 11 | 0 | 3 |
| Epistaxis | | | |
| subjects affected / exposed | 15 / 115 (13.04%) | 3 / 36 (8.33%) | 2 / 104 (1.92%) |
| occurrences (all) | 23 | 3 | 2 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 8 / 115 (6.96%) | 0 / 36 (0.00%) | 0 / 104 (0.00%) |
| occurrences (all) | 8 | 0 | 0 |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 8 / 115 (6.96%) | 2 / 36 (5.56%) | 4 / 104 (3.85%) |
| occurrences (all) | 11 | 2 | 8 |
| Confusional state | | | |
| subjects affected / exposed | 7 / 115 (6.09%) | 2 / 36 (5.56%) | 3 / 104 (2.88%) |
| occurrences (all) | 8 | 2 | 4 |
| Depression | | | |
| subjects affected / exposed | 13 / 115 (11.30%) | 4 / 36 (11.11%) | 15 / 104 (14.42%) |
| occurrences (all) | 17 | 4 | 18 |
| Insomnia | | | |
| subjects affected / exposed | 13 / 115 (11.30%) | 2 / 36 (5.56%) | 15 / 104 (14.42%) |
| occurrences (all) | 19 | 3 | 21 |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 9 / 115 (7.83%) | 1 / 36 (2.78%) | 3 / 104 (2.88%) |
| occurrences (all) | 14 | 1 | 3 |
| Aspartate aminotransferase increased | | | |

| | | | |
|-------------------------------------|-------------------|------------------|-------------------|
| subjects affected / exposed | 6 / 115 (5.22%) | 1 / 36 (2.78%) | 1 / 104 (0.96%) |
| occurrences (all) | 8 | 1 | 1 |
| Blood creatinine increased | | | |
| subjects affected / exposed | 6 / 115 (5.22%) | 2 / 36 (5.56%) | 1 / 104 (0.96%) |
| occurrences (all) | 9 | 4 | 3 |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 15 / 115 (13.04%) | 3 / 36 (8.33%) | 2 / 104 (1.92%) |
| occurrences (all) | 32 | 7 | 2 |
| Glycosylated haemoglobin increased | | | |
| subjects affected / exposed | 0 / 115 (0.00%) | 0 / 36 (0.00%) | 1 / 104 (0.96%) |
| occurrences (all) | 0 | 0 | 1 |
| Weight decreased | | | |
| subjects affected / exposed | 34 / 115 (29.57%) | 10 / 36 (27.78%) | 5 / 104 (4.81%) |
| occurrences (all) | 65 | 20 | 13 |
| Cardiac disorders | | | |
| Palpitations | | | |
| subjects affected / exposed | 7 / 115 (6.09%) | 1 / 36 (2.78%) | 6 / 104 (5.77%) |
| occurrences (all) | 10 | 2 | 7 |
| Nervous system disorders | | | |
| Amnesia | | | |
| subjects affected / exposed | 3 / 115 (2.61%) | 2 / 36 (5.56%) | 0 / 104 (0.00%) |
| occurrences (all) | 3 | 2 | 0 |
| Dizziness | | | |
| subjects affected / exposed | 21 / 115 (18.26%) | 3 / 36 (8.33%) | 13 / 104 (12.50%) |
| occurrences (all) | 37 | 3 | 16 |
| Dysgeusia | | | |
| subjects affected / exposed | 21 / 115 (18.26%) | 2 / 36 (5.56%) | 1 / 104 (0.96%) |
| occurrences (all) | 29 | 3 | 1 |
| Headache | | | |
| subjects affected / exposed | 29 / 115 (25.22%) | 7 / 36 (19.44%) | 23 / 104 (22.12%) |
| occurrences (all) | 87 | 8 | 30 |
| Hypoaesthesia | | | |
| subjects affected / exposed | 2 / 115 (1.74%) | 4 / 36 (11.11%) | 3 / 104 (2.88%) |
| occurrences (all) | 5 | 4 | 3 |
| Neuropathy peripheral | | | |

| | | | |
|--|----------------------|---------------------|----------------------|
| subjects affected / exposed occurrences (all) | 6 / 115 (5.22%) 7 | 3 / 36 (8.33%) 4 | 5 / 104 (4.81%) 5 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 8 / 115 (6.96%) | 3 / 36 (8.33%) | 9 / 104 (8.65%) |
| occurrences (all) | 13 | 5 | 13 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 5 / 115 (4.35%) | 2 / 36 (5.56%) | 1 / 104 (0.96%) |
| occurrences (all) | 10 | 3 | 1 |
| Ear and labyrinth disorders | | | |
| Deafness | | | |
| subjects affected / exposed | 7 / 115 (6.09%) | 2 / 36 (5.56%) | 0 / 104 (0.00%) |
| occurrences (all) | 8 | 4 | 0 |
| Ear pain | | | |
| subjects affected / exposed | 2 / 115 (1.74%) | 2 / 36 (5.56%) | 0 / 104 (0.00%) |
| occurrences (all) | 3 | 4 | 0 |
| Hypoacusis | | | |
| subjects affected / exposed | 6 / 115 (5.22%) | 1 / 36 (2.78%) | 0 / 104 (0.00%) |
| occurrences (all) | 7 | 1 | 0 |
| Tinnitus | | | |
| subjects affected / exposed | 7 / 115 (6.09%) | 0 / 36 (0.00%) | 2 / 104 (1.92%) |
| occurrences (all) | 13 | 0 | 2 |
| Vertigo | | | |
| subjects affected / exposed | 8 / 115 (6.96%) | 3 / 36 (8.33%) | 2 / 104 (1.92%) |
| occurrences (all) | 9 | 5 | 2 |
| Eye disorders | | | |
| Dry eye | | | |
| subjects affected / exposed | 7 / 115 (6.09%) | 1 / 36 (2.78%) | 4 / 104 (3.85%) |
| occurrences (all) | 8 | 2 | 4 |
| Eye pain | | | |
| subjects affected / exposed | 3 / 115 (2.61%) | 2 / 36 (5.56%) | 0 / 104 (0.00%) |
| occurrences (all) | 3 | 3 | 0 |
| Lacrimation increased | | | |
| subjects affected / exposed | 6 / 115 (5.22%) | 1 / 36 (2.78%) | 3 / 104 (2.88%) |
| occurrences (all) | 8 | 1 | 3 |
| Vision blurred | | | |

| | | | |
|--|----------------------|---------------------|----------------------|
| subjects affected / exposed occurrences (all) | 7 / 115 (6.09%) 8 | 2 / 36 (5.56%) 3 | 1 / 104 (0.96%) 1 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 12 / 115 (10.43%) | 3 / 36 (8.33%) | 11 / 104 (10.58%) |
| occurrences (all) | 17 | 4 | 12 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 9 / 115 (7.83%) | 1 / 36 (2.78%) | 6 / 104 (5.77%) |
| occurrences (all) | 12 | 2 | 8 |
| Constipation | | | |
| subjects affected / exposed | 29 / 115 (25.22%) | 8 / 36 (22.22%) | 16 / 104 (15.38%) |
| occurrences (all) | 39 | 9 | 23 |
| Diarrhoea | | | |
| subjects affected / exposed | 37 / 115 (32.17%) | 8 / 36 (22.22%) | 22 / 104 (21.15%) |
| occurrences (all) | 66 | 14 | 42 |
| Dry mouth | | | |
| subjects affected / exposed | 15 / 115 (13.04%) | 2 / 36 (5.56%) | 5 / 104 (4.81%) |
| occurrences (all) | 17 | 2 | 5 |
| Dyspepsia | | | |
| subjects affected / exposed | 9 / 115 (7.83%) | 4 / 36 (11.11%) | 9 / 104 (8.65%) |
| occurrences (all) | 11 | 4 | 12 |
| Dysphagia | | | |
| subjects affected / exposed | 3 / 115 (2.61%) | 2 / 36 (5.56%) | 0 / 104 (0.00%) |
| occurrences (all) | 3 | 2 | 0 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 4 / 115 (3.48%) | 2 / 36 (5.56%) | 1 / 104 (0.96%) |
| occurrences (all) | 5 | 3 | 1 |
| Haemorrhoids | | | |
| subjects affected / exposed | 6 / 115 (5.22%) | 2 / 36 (5.56%) | 2 / 104 (1.92%) |
| occurrences (all) | 8 | 3 | 2 |
| Nausea | | | |
| subjects affected / exposed | 35 / 115 (30.43%) | 8 / 36 (22.22%) | 19 / 104 (18.27%) |
| occurrences (all) | 66 | 9 | 31 |
| Stomatitis | | | |
| subjects affected / exposed | 8 / 115 (6.96%) | 4 / 36 (11.11%) | 0 / 104 (0.00%) |
| occurrences (all) | 15 | 5 | 0 |

| | | | |
|--|-------------------------|------------------------|-------------------------|
| Toothache subjects affected / exposed occurrences (all) | 10 / 115 (8.70%) 11 | 2 / 36 (5.56%) 3 | 1 / 104 (0.96%) 1 |
| Vomiting subjects affected / exposed occurrences (all) | 23 / 115 (20.00%) 32 | 4 / 36 (11.11%) 4 | 6 / 104 (5.77%) 8 |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia subjects affected / exposed occurrences (all) | 16 / 115 (13.91%) 20 | 2 / 36 (5.56%) 3 | 8 / 104 (7.69%) 12 |
| Dry skin subjects affected / exposed occurrences (all) | 15 / 115 (13.04%) 20 | 2 / 36 (5.56%) 2 | 3 / 104 (2.88%) 3 |
| Hypertrichosis subjects affected / exposed occurrences (all) | 2 / 115 (1.74%) 3 | 2 / 36 (5.56%) 2 | 0 / 104 (0.00%) 0 |
| Onychoclasia subjects affected / exposed occurrences (all) | 25 / 115 (21.74%) 33 | 11 / 36 (30.56%) 16 | 1 / 104 (0.96%) 1 |
| Pruritus subjects affected / exposed occurrences (all) | 16 / 115 (13.91%) 23 | 2 / 36 (5.56%) 3 | 6 / 104 (5.77%) 6 |
| Rash subjects affected / exposed occurrences (all) | 7 / 115 (6.09%) 11 | 0 / 36 (0.00%) 0 | 4 / 104 (3.85%) 4 |
| Skin lesion subjects affected / exposed occurrences (all) | 1 / 115 (0.87%) 1 | 2 / 36 (5.56%) 2 | 3 / 104 (2.88%) 4 |
| Renal and urinary disorders | | | |
| Dysuria subjects affected / exposed occurrences (all) | 11 / 115 (9.57%) 17 | 1 / 36 (2.78%) 1 | 1 / 104 (0.96%) 1 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia subjects affected / exposed occurrences (all) | 29 / 115 (25.22%) 61 | 10 / 36 (27.78%) 18 | 41 / 104 (39.42%) 80 |

| | | | |
|-----------------------------|-------------------|------------------|-------------------|
| Back pain | | | |
| subjects affected / exposed | 30 / 115 (26.09%) | 6 / 36 (16.67%) | 18 / 104 (17.31%) |
| occurrences (all) | 48 | 12 | 30 |
| Bone pain | | | |
| subjects affected / exposed | 7 / 115 (6.09%) | 3 / 36 (8.33%) | 11 / 104 (10.58%) |
| occurrences (all) | 9 | 3 | 18 |
| Flank pain | | | |
| subjects affected / exposed | 5 / 115 (4.35%) | 2 / 36 (5.56%) | 3 / 104 (2.88%) |
| occurrences (all) | 6 | 2 | 5 |
| Joint stiffness | | | |
| subjects affected / exposed | 3 / 115 (2.61%) | 0 / 36 (0.00%) | 3 / 104 (2.88%) |
| occurrences (all) | 4 | 0 | 3 |
| Muscle spasms | | | |
| subjects affected / exposed | 41 / 115 (35.65%) | 12 / 36 (33.33%) | 4 / 104 (3.85%) |
| occurrences (all) | 69 | 18 | 5 |
| Muscular weakness | | | |
| subjects affected / exposed | 6 / 115 (5.22%) | 0 / 36 (0.00%) | 1 / 104 (0.96%) |
| occurrences (all) | 8 | 0 | 1 |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 7 / 115 (6.09%) | 2 / 36 (5.56%) | 10 / 104 (9.62%) |
| occurrences (all) | 11 | 2 | 18 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 18 / 115 (15.65%) | 5 / 36 (13.89%) | 15 / 104 (14.42%) |
| occurrences (all) | 28 | 8 | 23 |
| Myalgia | | | |
| subjects affected / exposed | 11 / 115 (9.57%) | 2 / 36 (5.56%) | 9 / 104 (8.65%) |
| occurrences (all) | 22 | 2 | 9 |
| Neck pain | | | |
| subjects affected / exposed | 9 / 115 (7.83%) | 1 / 36 (2.78%) | 7 / 104 (6.73%) |
| occurrences (all) | 15 | 1 | 9 |
| Pain in extremity | | | |
| subjects affected / exposed | 19 / 115 (16.52%) | 7 / 36 (19.44%) | 16 / 104 (15.38%) |
| occurrences (all) | 24 | 11 | 30 |
| Pain in jaw | | | |
| subjects affected / exposed | 1 / 115 (0.87%) | 2 / 36 (5.56%) | 2 / 104 (1.92%) |
| occurrences (all) | 1 | 3 | 2 |

| | | | |
|--|---|---|--|
| Infections and infestations Cystitis subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) Sinusitis subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all) | 6 / 115 (5.22%) 9 13 / 115 (11.30%) 17 6 / 115 (5.22%) 6 7 / 115 (6.09%) 10 21 / 115 (18.26%) 35 | 0 / 36 (0.00%) 0 0 / 36 (0.00%) 0 1 / 36 (2.78%) 1 0 / 36 (0.00%) 0 3 / 36 (8.33%) 3 | 5 / 104 (4.81%) 8 9 / 104 (8.65%) 13 2 / 104 (1.92%) 2 7 / 104 (6.73%) 7 8 / 104 (7.69%) 10 |
| Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all) Dehydration subjects affected / exposed occurrences (all) Hyperglycaemia subjects affected / exposed occurrences (all) Hyperuricaemia subjects affected / exposed occurrences (all) | 41 / 115 (35.65%) 64 1 / 115 (0.87%) 1 50 / 115 (43.48%) 134 4 / 115 (3.48%) 4 | 13 / 36 (36.11%) 25 0 / 36 (0.00%) 0 9 / 36 (25.00%) 23 0 / 36 (0.00%) 0 | 13 / 104 (12.50%) 20 1 / 104 (0.96%) 1 4 / 104 (3.85%) 23 0 / 104 (0.00%) 0 |

| | | | |
|--|--|--|--|
| Non-serious adverse events | CP-751,871 + Exemestane (after Exemestane) | | |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 43 / 43 (100.00%) | | |
| Vascular disorders | | | |
| Hot flush | | | |

| | | | |
|--|------------------|--|--|
| subjects affected / exposed | 7 / 43 (16.28%) | | |
| occurrences (all) | 13 | | |
| Hypertension | | | |
| subjects affected / exposed | 3 / 43 (6.98%) | | |
| occurrences (all) | 3 | | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 8 / 43 (18.60%) | | |
| occurrences (all) | 10 | | |
| Chest pain | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences (all) | 2 | | |
| Fatigue | | | |
| subjects affected / exposed | 16 / 43 (37.21%) | | |
| occurrences (all) | 36 | | |
| Influenza like illness | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Injection site pain | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Oedema peripheral | | | |
| subjects affected / exposed | 3 / 43 (6.98%) | | |
| occurrences (all) | 3 | | |
| Pain | | | |
| subjects affected / exposed | 6 / 43 (13.95%) | | |
| occurrences (all) | 15 | | |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences (all) | 1 | | |
| Reproductive system and breast disorders | | | |
| Breast pain | | | |
| subjects affected / exposed | 5 / 43 (11.63%) | | |
| occurrences (all) | 6 | | |
| Pelvic pain | | | |

| | | | |
|---|------------------|--|--|
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences (all) | 1 | | |
| Vulvovaginal dryness | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences (all) | 1 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 7 / 43 (16.28%) | | |
| occurrences (all) | 7 | | |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences (all) | 1 | | |
| Epistaxis | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences (all) | 1 | | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 3 / 43 (6.98%) | | |
| occurrences (all) | 3 | | |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 3 / 43 (6.98%) | | |
| occurrences (all) | 9 | | |
| Confusional state | | | |
| subjects affected / exposed | 2 / 43 (4.65%) | | |
| occurrences (all) | 3 | | |
| Depression | | | |
| subjects affected / exposed | 12 / 43 (27.91%) | | |
| occurrences (all) | 22 | | |
| Insomnia | | | |
| subjects affected / exposed | 5 / 43 (11.63%) | | |
| occurrences (all) | 12 | | |
| Investigations | | | |

| | | | |
|--|------------------------|--|--|
| Alanine aminotransferase increased subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | | |
| Aspartate aminotransferase increased subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | | |
| Blood creatinine increased subjects affected / exposed occurrences (all) | 2 / 43 (4.65%) 3 | | |
| Gamma-glutamyltransferase increased subjects affected / exposed occurrences (all) | 2 / 43 (4.65%) 3 | | |
| Glycosylated haemoglobin increased subjects affected / exposed occurrences (all) | 3 / 43 (6.98%) 5 | | |
| Weight decreased subjects affected / exposed occurrences (all) | 14 / 43 (32.56%) 28 | | |
| Cardiac disorders Palpitations subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | | |
| Nervous system disorders Amnesia subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | | |
| Dizziness subjects affected / exposed occurrences (all) | 6 / 43 (13.95%) 6 | | |
| Dysgeusia subjects affected / exposed occurrences (all) | 7 / 43 (16.28%) 10 | | |
| Headache subjects affected / exposed occurrences (all) | 13 / 43 (30.23%) 14 | | |
| Hypoaesthesia | | | |

| | | | |
|--------------------------------------|-----------------|--|--|
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences (all) | 1 | | |
| Neuropathy peripheral | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences (all) | 2 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 5 / 43 (11.63%) | | |
| occurrences (all) | 6 | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences (all) | 1 | | |
| Ear and labyrinth disorders | | | |
| Deafness | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Ear pain | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hypoacusis | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Tinnitus | | | |
| subjects affected / exposed | 2 / 43 (4.65%) | | |
| occurrences (all) | 3 | | |
| Vertigo | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Eye disorders | | | |
| Dry eye | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences (all) | 2 | | |
| Eye pain | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences (all) | 2 | | |
| Lacrimation increased | | | |

| | | | |
|----------------------------------|------------------|--|--|
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences (all) | 1 | | |
| Vision blurred | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences (all) | 1 | | |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 3 / 43 (6.98%) | | |
| occurrences (all) | 4 | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 3 / 43 (6.98%) | | |
| occurrences (all) | 4 | | |
| Constipation | | | |
| subjects affected / exposed | 7 / 43 (16.28%) | | |
| occurrences (all) | 13 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 12 / 43 (27.91%) | | |
| occurrences (all) | 22 | | |
| Dry mouth | | | |
| subjects affected / exposed | 5 / 43 (11.63%) | | |
| occurrences (all) | 6 | | |
| Dyspepsia | | | |
| subjects affected / exposed | 3 / 43 (6.98%) | | |
| occurrences (all) | 4 | | |
| Dysphagia | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences (all) | 1 | | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 2 / 43 (4.65%) | | |
| occurrences (all) | 3 | | |
| Haemorrhoids | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences (all) | 1 | | |
| Nausea | | | |
| subjects affected / exposed | 15 / 43 (34.88%) | | |
| occurrences (all) | 24 | | |

| | | | |
|---|-----------------|--|--|
| Stomatitis | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences (all) | 1 | | |
| Toothache | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Vomiting | | | |
| subjects affected / exposed | 7 / 43 (16.28%) | | |
| occurrences (all) | 20 | | |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia | | | |
| subjects affected / exposed | 3 / 43 (6.98%) | | |
| occurrences (all) | 4 | | |
| Dry skin | | | |
| subjects affected / exposed | 2 / 43 (4.65%) | | |
| occurrences (all) | 3 | | |
| Hypertrichosis | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Onychoclasia | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pruritus | | | |
| subjects affected / exposed | 4 / 43 (9.30%) | | |
| occurrences (all) | 9 | | |
| Rash | | | |
| subjects affected / exposed | 2 / 43 (4.65%) | | |
| occurrences (all) | 4 | | |
| Skin lesion | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences (all) | 2 | | |
| Renal and urinary disorders | | | |
| Dysuria | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|-----------------------------|------------------|--|--|
| Arthralgia | | | |
| subjects affected / exposed | 16 / 43 (37.21%) | | |
| occurrences (all) | 25 | | |
| Back pain | | | |
| subjects affected / exposed | 11 / 43 (25.58%) | | |
| occurrences (all) | 21 | | |
| Bone pain | | | |
| subjects affected / exposed | 4 / 43 (9.30%) | | |
| occurrences (all) | 5 | | |
| Flank pain | | | |
| subjects affected / exposed | 3 / 43 (6.98%) | | |
| occurrences (all) | 5 | | |
| Joint stiffness | | | |
| subjects affected / exposed | 3 / 43 (6.98%) | | |
| occurrences (all) | 4 | | |
| Muscle spasms | | | |
| subjects affected / exposed | 8 / 43 (18.60%) | | |
| occurrences (all) | 24 | | |
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 7 / 43 (16.28%) | | |
| occurrences (all) | 16 | | |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 9 / 43 (20.93%) | | |
| occurrences (all) | 13 | | |
| Myalgia | | | |
| subjects affected / exposed | 9 / 43 (20.93%) | | |
| occurrences (all) | 10 | | |
| Neck pain | | | |
| subjects affected / exposed | 5 / 43 (11.63%) | | |
| occurrences (all) | 8 | | |
| Pain in extremity | | | |
| subjects affected / exposed | 8 / 43 (18.60%) | | |
| occurrences (all) | 18 | | |

| | | | |
|---|--|--|--|
| Pain in jaw subjects affected / exposed occurrences (all) | 2 / 43 (4.65%) 3 | | |
| Infections and infestations Cystitis subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) Sinusitis subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all) | 3 / 43 (6.98%) 3 0 / 43 (0.00%) 0 0 / 43 (0.00%) 0 2 / 43 (4.65%) 2 8 / 43 (18.60%) 8 | | |
| Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all) Dehydration subjects affected / exposed occurrences (all) Hyperglycaemia subjects affected / exposed occurrences (all) Hyperuricaemia subjects affected / exposed occurrences (all) | 13 / 43 (30.23%) 18 3 / 43 (6.98%) 3 9 / 43 (20.93%) 20 3 / 43 (6.98%) 4 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 21 December 2009 | 1. Patients with any history of unstable angina, myocardial infarction or symptomatic congestive heart failure were to be excluded from study entry. In addition, future patients with a requirement for inotropic support or serious uncontrolled cardiac arrhythmia (including atrial flutter/fibrillation) within 3 years prior to screening would be excluded from study entry. Patients requiring the use of pacemakers and/or implanted defibrillators were excluded from study participations. 2. Patients must have a screening hemoglobin A1C lower than 5.7% for their inclusion. |
| 09 December 2010 | 1. Stop collection of blood samples for circulating tumor cell evaluation, biomarker analysis, PK and HAHA analysis. 2. Patients who experienced disease progression would no longer be allowed to routinely cross over to receive Salvage Therapy. |
| 19 June 2012 | Definition of adverse event updated to include addition of medication error. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported