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	• 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 text. 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)

	Scores

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 â€˜Not at Allâ€™ to 4 â€˜Very Muchâ€™). 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+Exemestan	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+Exemestan	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	14 / 115 (12.17%)	3 / 36 (8.33%)	4 / 104 (3.85%)
occurrences (all)	17	6	6
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	17 / 115 (14.78%)	3 / 36 (8.33%)	13 / 104 (12.50%)
occurrences (all)	28	5	18
Chest pain			
subjects affected / exposed	8 / 115 (6.96%)	2 / 36 (5.56%)	8 / 104 (7.69%)
occurrences (all)	11	3	10
Fatigue			
subjects affected / exposed	35 / 115 (30.43%)	11 / 36 (30.56%)	33 / 104 (31.73%)
occurrences (all)	66	17	57
Influenza like illness			
subjects affected / exposed	6 / 115 (5.22%)	1 / 36 (2.78%)	2 / 104 (1.92%)
occurrences (all)	7	1	2
Injection site pain			
subjects affected / exposed	0 / 115 (0.00%)	2 / 36 (5.56%)	0 / 104 (0.00%)
occurrences (all)	0	2	0
Oedema peripheral			
subjects affected / exposed	5 / 115 (4.35%)	1 / 36 (2.78%)	10 / 104 (9.62%)
occurrences (all)	7	2	19
Pain			
subjects affected / exposed	7 / 115 (6.09%)	2 / 36 (5.56%)	8 / 104 (7.69%)
occurrences (all)	10	2	10
Pyrexia			
subjects affected / exposed	11 / 115 (9.57%)	1 / 36 (2.78%)	5 / 104 (4.81%)
occurrences (all)	13	1	5
Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	6 / 115 (5.22%)	2 / 36 (5.56%)	10 / 104 (9.62%)
occurrences (all)	8	5	15
Pelvic pain			
subjects affected / exposed	4 / 115 (3.48%)	2 / 36 (5.56%)	3 / 104 (2.88%)
occurrences (all)	5	2	4
Vulvovaginal dryness			

subjects affected / exposed	6 / 115 (5.22%)	3 / 36 (8.33%)	3 / 104 (2.88%)
occurrences (all)	6	4	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	6 / 115 (5.22%)	3 / 36 (8.33%)	5 / 104 (4.81%)
occurrences (all)	7	4	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	7 / 115 (6.09%)	2 / 36 (5.56%)	1 / 104 (0.96%)
occurrences (all)	8	3	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	10 / 115 (8.70%)	2 / 36 (5.56%)	1 / 104 (0.96%)
occurrences (all)	11	3	1
Vomiting			
subjects affected / exposed	23 / 115 (20.00%)	4 / 36 (11.11%)	6 / 104 (5.77%)
occurrences (all)	32	4	8
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	16 / 115 (13.91%)	2 / 36 (5.56%)	8 / 104 (7.69%)
occurrences (all)	20	3	12
Dry skin			
subjects affected / exposed	15 / 115 (13.04%)	2 / 36 (5.56%)	3 / 104 (2.88%)
occurrences (all)	20	2	3
Hypertrichosis			
subjects affected / exposed	2 / 115 (1.74%)	2 / 36 (5.56%)	0 / 104 (0.00%)
occurrences (all)	3	2	0
Onychoclasis			
subjects affected / exposed	25 / 115 (21.74%)	11 / 36 (30.56%)	1 / 104 (0.96%)
occurrences (all)	33	16	1
Pruritus			
subjects affected / exposed	16 / 115 (13.91%)	2 / 36 (5.56%)	6 / 104 (5.77%)
occurrences (all)	23	3	6
Rash			
subjects affected / exposed	7 / 115 (6.09%)	0 / 36 (0.00%)	4 / 104 (3.85%)
occurrences (all)	11	0	4
Skin lesion			
subjects affected / exposed	1 / 115 (0.87%)	2 / 36 (5.56%)	3 / 104 (2.88%)
occurrences (all)	1	2	4
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	11 / 115 (9.57%)	1 / 36 (2.78%)	1 / 104 (0.96%)
occurrences (all)	17	1	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	29 / 115 (25.22%)	10 / 36 (27.78%)	41 / 104 (39.42%)
occurrences (all)	61	18	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	6 / 115 (5.22%)	0 / 36 (0.00%)	5 / 104 (4.81%)
occurrences (all)	9	0	8
Nasopharyngitis			
subjects affected / exposed	13 / 115 (11.30%)	0 / 36 (0.00%)	9 / 104 (8.65%)
occurrences (all)	17	0	13
Sinusitis			
subjects affected / exposed	6 / 115 (5.22%)	1 / 36 (2.78%)	2 / 104 (1.92%)
occurrences (all)	6	1	2
Upper respiratory tract infection			
subjects affected / exposed	7 / 115 (6.09%)	0 / 36 (0.00%)	7 / 104 (6.73%)
occurrences (all)	10	0	7
Urinary tract infection			
subjects affected / exposed	21 / 115 (18.26%)	3 / 36 (8.33%)	8 / 104 (7.69%)
occurrences (all)	35	3	10
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	41 / 115 (35.65%)	13 / 36 (36.11%)	13 / 104 (12.50%)
occurrences (all)	64	25	20
Dehydration			
subjects affected / exposed	1 / 115 (0.87%)	0 / 36 (0.00%)	1 / 104 (0.96%)
occurrences (all)	1	0	1
Hyperglycaemia			
subjects affected / exposed	50 / 115 (43.48%)	9 / 36 (25.00%)	4 / 104 (3.85%)
occurrences (all)	134	23	23
Hyperuricaemia			
subjects affected / exposed	4 / 115 (3.48%)	0 / 36 (0.00%)	0 / 104 (0.00%)
occurrences (all)	4	0	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	0 / 43 (0.00%)		
occurrences (all)	0		
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences (all)	0		
Blood creatinine increased			
subjects affected / exposed	2 / 43 (4.65%)		
occurrences (all)	3		
Gamma-glutamyltransferase increased			
subjects affected / exposed	2 / 43 (4.65%)		
occurrences (all)	3		
Glycosylated haemoglobin increased			
subjects affected / exposed	3 / 43 (6.98%)		
occurrences (all)	5		
Weight decreased			
subjects affected / exposed	14 / 43 (32.56%)		
occurrences (all)	28		
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Amnesia			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences (all)	0		
Dizziness			
subjects affected / exposed	6 / 43 (13.95%)		
occurrences (all)	6		
Dysgeusia			
subjects affected / exposed	7 / 43 (16.28%)		
occurrences (all)	10		
Headache			
subjects affected / exposed	13 / 43 (30.23%)		
occurrences (all)	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 occurrences (all)	1 / 43 (2.33%) 1		
Toothache subjects affected / exposed occurrences (all)	0 / 43 (0.00%) 0		
Vomiting subjects affected / exposed occurrences (all)	7 / 43 (16.28%) 20		
Skin and subcutaneous tissue disorders			
Alopecia subjects affected / exposed occurrences (all)	3 / 43 (6.98%) 4		
Dry skin subjects affected / exposed occurrences (all)	2 / 43 (4.65%) 3		
Hypertrichosis subjects affected / exposed occurrences (all)	0 / 43 (0.00%) 0		
Onychoclasis subjects affected / exposed occurrences (all)	0 / 43 (0.00%) 0		
Pruritus subjects affected / exposed occurrences (all)	4 / 43 (9.30%) 9		
Rash subjects affected / exposed occurrences (all)	2 / 43 (4.65%) 4		
Skin lesion subjects affected / exposed occurrences (all)	1 / 43 (2.33%) 2		
Renal and urinary disorders			
Dysuria subjects affected / exposed occurrences (all)	0 / 43 (0.00%) 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