



Clinical trial results:

Randomized, Open-Label Study of Abiraterone Acetate (JNJ-212082) Plus Prednisone With or Without Exemestane in Postmenopausal Women With ER+ Metastatic Breast Cancer Progressing After Letrozole or Anastrozole Therapy

Summary

EudraCT number	2011-000621-80
Trial protocol	BE GB ES FR NL IE IT PL
Global end of trial date	08 August 2018

Results information

Result version number	v1 (current)
This version publication date	22 August 2019
First version publication date	22 August 2019

Trial information

Trial identification

Sponsor protocol code	212082BCA2001
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01381874
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Research & Development, LLC
Sponsor organisation address	920 Route 202, Raritan, United States, NJ 08869
Public contact	Clinical Registry group, Janssen Research & Development, LLC, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry group, Janssen Research & Development, LLC, ClinicalTrialsEU@its.jnj.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	08 August 2018
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	08 August 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to assess safety and efficacy of abiraterone acetate plus prednisone (AAP) and abiraterone acetate plus prednisone plus exemestane (AAPE), each compared with exemestane (E) alone, in postmenopausal women with estrogen receptor positive (ER+) metastatic breast cancer progressing after letrozole or anastrozole therapy.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practices and applicable regulatory requirements. Safety and tolerability were evaluated by examining the incidence and type of adverse events (AEs), and changes in clinical laboratory test values, vital signs measurements, and physical examination. Cardiac function was assessed by multi-gated acquisition (MUGA) scan or echocardiogram (ECHO) and 12-lead electrocardiogram (ECG).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 August 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 60
Country: Number of subjects enrolled	Spain: 30
Country: Number of subjects enrolled	France: 41
Country: Number of subjects enrolled	United Kingdom: 30
Country: Number of subjects enrolled	Italy: 5
Country: Number of subjects enrolled	Korea, Republic of: 6
Country: Number of subjects enrolled	Netherlands: 21
Country: Number of subjects enrolled	Russian Federation: 51
Country: Number of subjects enrolled	Ukraine: 25
Country: Number of subjects enrolled	United States: 28
Worldwide total number of subjects	297
EEA total number of subjects	187

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	167
From 65 to 84 years	129
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total 297 subjects were enrolled and 102 subjects were randomized in the exemestane (E), 89 in the abiraterone acetate plus prednisone (AAP) group, and 106 in the abiraterone acetate plus prednisone plus exemestane (AAPE) group. Out of this 293 subjects were treated (102 [E group], 87 [AAPE group], and 104 subjects [AAPE group], respectively).

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
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Arm title	Exemestane (E)
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Arm description:

Subjects received exemestane tablet as oral dose of 25 milligram (mg) once daily in 28-day treatment cycles until disease progression, unacceptable toxicity, or death (up to 3 years).

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:

Subjects received 25 mg exemestane once daily in 28-day treatment cycles until disease progression, unacceptable toxicity, or death (up to 3 years).

Arm title	Abiraterone Acetate plus Prednisone (AAP)
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Arm description:

Subjects received abiraterone acetate tablet at a total oral dose of 1000 mg along with 5 mg capsule of prednisone/prednisolone once daily in 28-day treatment cycles until disease progression, unacceptable toxicity, or death (up to 3 years).

Arm type	Experimental
Investigational medicinal product name	Abiraterone acetate
Investigational medicinal product code	
Other name	JNJ-212082
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received 1000 mg abiraterone acetate once daily in 28-day treatment cycles until disease progression, unacceptable toxicity, or death (up to 3 years).

Investigational medicinal product name	Prednisone/Prednisolone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects received 5 mg prednisone/prednisolone once daily in 28-day treatment cycles until disease progression, unacceptable toxicity, or death (up to 3 years).

Arm title	Abiraterone Acetate plus Prednisone plus Exemestane (AAPE)
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Arm description:

Subjects received abiraterone acetate tablet at a total oral dose of 1000 mg and 5 mg capsule of prednisone/prednisolone along with exemestane tablet 25 mg once daily in 28-day treatment cycles until disease progression, unacceptable toxicity, or death (up to 3 years).

Arm type	Experimental
Investigational medicinal product name	Abiraterone acetate
Investigational medicinal product code	
Other name	JNJ-212082
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received 1000 mg abiraterone acetate once daily in 28 day treatment cycles until disease progression, unacceptable toxicity, or death (up to 3 years).

Investigational medicinal product name	Exemestane
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received 25 mg exemestane once daily in 28-day treatment cycles until disease progression, unacceptable toxicity, or death (up to 3 years).

Investigational medicinal product name	Prednisone/prednisolone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects received 5 mg prednisone/prednisolone once daily in 28-day treatment cycles until disease progression, unacceptable toxicity, or death (up to 3 years).

Number of subjects in period 1	Exemestane (E)	Abiraterone Acetate plus Prednisone (AAP)	Abiraterone Acetate plus Prednisone plus Exemestane (AAPE)
Started	102	89	106
Treated	102	87	104
Completed	0	0	0
Not completed	102	89	106
Adverse event, serious fatal	24	26	29
Consent withdrawn by subject	9	10	9
Physician decision	1	-	1
Other	67	52	67
Lost to follow-up	1	1	-

Baseline characteristics

Reporting groups

Reporting group title	Exemestane (E)
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Reporting group description:

Subjects received exemestane tablet as oral dose of 25 milligram (mg) once daily in 28-day treatment cycles until disease progression, unacceptable toxicity, or death (up to 3 years).

Reporting group title	Abiraterone Acetate plus Prednisone (AAP)
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Reporting group description:

Subjects received abiraterone acetate tablet at a total oral dose of 1000 mg along with 5 mg capsule of prednisone/prednisolone once daily in 28-day treatment cycles until disease progression, unacceptable toxicity, or death (up to 3 years).

Reporting group title	Abiraterone Acetate plus Prednisone plus Exemestane (AAPE)
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Reporting group description:

Subjects received abiraterone acetate tablet at a total oral dose of 1000 mg and 5 mg capsule of prednisone/prednisolone along with exemestane tablet 25 mg once daily in 28-day treatment cycles until disease progression, unacceptable toxicity, or death (up to 3 years).

Reporting group values	Exemestane (E)	Abiraterone Acetate plus Prednisone (AAP)	Abiraterone Acetate plus Prednisone plus Exemestane (AAPE)
Number of subjects	102	89	106
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	60	54	53
From 65 to 84 years	42	35	52
85 years and over	0	0	1
Title for AgeContinuous Units: years			
arithmetic mean	61.9	63.1	63.8
standard deviation	± 8.55	± 9.17	± 10.91
Title for Gender Units: subjects			
Female	102	89	106

Reporting group values	Total		
Number of subjects	297		
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	167		
From 65 to 84 years	129		
85 years and over	1		
Title for AgeContinuous Units: years			
arithmetic mean	-		
standard deviation	-		

Title for Gender			
Units: subjects			
Female	297		

End points

End points reporting groups

Reporting group title	Exemestane (E)
Reporting group description: Subjects received exemestane tablet as oral dose of 25 milligram (mg) once daily in 28-day treatment cycles until disease progression, unacceptable toxicity, or death (up to 3 years).	
Reporting group title	Abiraterone Acetate plus Prednisone (AAP)
Reporting group description: Subjects received abiraterone acetate tablet at a total oral dose of 1000 mg along with 5 mg capsule of prednisone/prednisolone once daily in 28-day treatment cycles until disease progression, unacceptable toxicity, or death (up to 3 years).	
Reporting group title	Abiraterone Acetate plus Prednisone plus Exemestane (AAPE)
Reporting group description: Subjects received abiraterone acetate tablet at a total oral dose of 1000 mg and 5 mg capsule of prednisone/prednisolone along with exemestane tablet 25 mg once daily in 28-day treatment cycles until disease progression, unacceptable toxicity, or death (up to 3 years).	

Primary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)
End point description: Progression-free survival was defined as the time from randomization to first occurrence of disease progression (either radiographic or clinical), or death from any cause. PFS was determined using radiographic progression defined by Response Evaluation Criteria in Solid Tumors (RECIST) on measurable lesions captured by computed tomography (CT) or magnetic resonance imaging (MRI). Clinical disease progression was considered only when disease progression could not be confirmed by CT or MRI, such as when the disease site is skin, bone marrow, or central nervous system. Intent-to-Treat (ITT) analysis set included all subjects randomized into the study.	
End point type	Primary
End point timeframe: Approximately 2 years	

End point values	Exemestane (E)	Abiraterone Acetate plus Prednisone (AAP)	Abiraterone Acetate plus Prednisone plus Exemestane (AAPE)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	102	89	106	
Units: Months				
median (confidence interval 95%)	3.68 (1.94 to 5.26)	3.65 (2.73 to 5.59)	4.47 (3.68 to 5.59)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Abiraterone Acetate plus Prednisone (AAP) v Exemestane (E)
Number of subjects included in analysis	191
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.437
Method	Stratified log-rank test
Parameter estimate	Hazard ratio (HR)
Point estimate	1.143
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.816
upper limit	1.603

Statistical analysis title	Statistical Analysis 2
Comparison groups	Exemestane (E) v Abiraterone Acetate plus Prednisone plus Exemestane (AAPE)
Number of subjects included in analysis	208
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.794
Method	Stratified log-rank test
Parameter estimate	Hazard ratio (HR)
Point estimate	0.958
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.695
upper limit	1.32

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)
End point description:	
Overall Survival was calculated as the time from randomization to death from any cause. ITT analysis set included all subjects randomized into the study. Here '99999' represents that median (arm E and AAPE), lower limit (arm E and AAPE) and upper limit of confidence interval (CI) (arm E, AAP and AAPE) were not estimable due to lesser number of events (high rate of censoring).	
End point type	Secondary
End point timeframe:	
Approximately 3 years	

End point values	Exemestane (E)	Abiraterone Acetate plus Prednisone (AAP)	Abiraterone Acetate plus Prednisone plus Exemestane (AAPE)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	102	89	106	
Units: Months				
median (confidence interval 95%)	99999 (99999 to 99999)	26.41 (23.49 to 99999)	99999 (23.79 to 99999)	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Abiraterone Acetate plus Prednisone (AAP) v Exemestane (E)
Number of subjects included in analysis	191
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.807
Method	Stratified log-rank test
Parameter estimate	Hazard ratio (HR)
Point estimate	1.074
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.608
upper limit	1.896

Statistical analysis title	Statistical Analysis 2
Comparison groups	Exemestane (E) v Abiraterone Acetate plus Prednisone plus Exemestane (AAPE)
Number of subjects included in analysis	208
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.542
Method	Stratified log-rank test
Parameter estimate	Hazard ratio (HR)
Point estimate	1.183
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.688
upper limit	2.036

Secondary: Overall Response Rate (ORR)

End point title	Overall Response Rate (ORR)
End point description:	
Overall response rate was defined as the percentage of subjects with measurable disease achieving a best overall response of either complete response (CR) or partial response (PR) based on RECIST. CR: disappearance of all target lesions and non-target lesions. PR: at least a 30 percent (%) decrease in the sum of longest diameter (LD) of target lesions or persistence of one or more non-target lesion(s) or/and maintenance of tumor marker level above the normal limits. ITT analysis set (all subjects randomized into the study) with measurable disease at baseline.	
End point type	Secondary
End point timeframe:	
Approximately 2 years	

End point values	Exemestane (E)	Abiraterone Acetate plus Prednisone (AAP)	Abiraterone Acetate plus Prednisone plus Exemestane (AAPE)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	63	52	66	
Units: Percentage of subjects				
number (not applicable)	6.3	5.8	12.1	

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Exemestane (E) v Abiraterone Acetate plus Prednisone (AAP)
Number of subjects included in analysis	115
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 1
Method	Fisher exact
Parameter estimate	Risk ratio (RR)
Point estimate	0.909
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.213
upper limit	3.878

Statistical analysis title	Statistical Analysis 2
Comparison groups	Exemestane (E) v Abiraterone Acetate plus Prednisone plus Exemestane (AAPE)

Number of subjects included in analysis	129
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.366
Method	Fisher exact
Parameter estimate	Risk ratio (RR)
Point estimate	1.909
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.605
upper limit	6.026

Secondary: Duration of Response

End point title	Duration of Response
End point description:	
Duration of objective response was measured from the first time that the CR or PR was achieved to the first observation of disease progression (either radiographic or clinical) based on the RECIST criteria. CR: disappearance of all target lesions and non target lesions. PR: at least a 30 percent (%) decrease in the sum of longest diameter (LD) of target lesions or persistence of one or more nontarget lesion(s) or/and maintenance of tumor marker level above the normal limits. ITT analysis set (all subjects randomized into the study) with measurable disease at baseline with complete or partial response. Here -99999 represents lower limit of CI (arm E) and '99999' represents that upper limit of CI (arm E, arm AAP and AAPE) were not estimable due to lesser number of events (high rate of censoring).	
End point type	Secondary
End point timeframe:	
Approximately 2 years	

End point values	Exemestane (E)	Abiraterone Acetate plus Prednisone (AAP)	Abiraterone Acetate plus Prednisone plus Exemestane (AAPE)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	4	3	8	
Units: Months				
median (confidence interval 95%)	6.47 (-99999 to 99999)	4.86 (4.63 to 99999)	6.93 (4.57 to 99999)	

Statistical analyses

Statistical analysis title	Statistical Analysis 2
Comparison groups	Exemestane (E) v Abiraterone Acetate plus Prednisone plus Exemestane (AAPE)

Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.625
Method	Stratified log-rank test
Parameter estimate	Hazard ratio (HR)
Point estimate	1.781
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.171
upper limit	18.493

Statistical analysis title	Statistical Analysis 1
Comparison groups	Exemestane (E) v Abiraterone Acetate plus Prednisone (AAP)
Number of subjects included in analysis	7
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.695
Method	Stratified log-rank test
Parameter estimate	Hazard ratio (HR)
Point estimate	1.618
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.143
upper limit	18.312

Secondary: Clinical Benefit Rate

End point title	Clinical Benefit Rate
End point description:	
Clinical benefit rate was defined as the percentage of subjects with measurable disease achieving a best overall response of a CR, PR, or stable disease (SD) for at least 6 months based on RECIST. Stable disease: neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for progressive disease (PD), taking as reference the smallest sum diameters while on study and persistence of one or more non-target lesion(s) and/or maintenance of tumour marker level above the normal limits. ITT analysis set with measurable disease at baseline.	
End point type	Secondary
End point timeframe:	
Approximately 2 years	

End point values	Exemestane (E)	Abiraterone Acetate plus Prednisone (AAP)	Abiraterone Acetate plus Prednisone plus Exemestane (AAPE)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	63	52	66	
Units: Percentage of subjects				
number (not applicable)	12.7	9.6	22.7	

Statistical analyses

Statistical analysis title	Statistical Analysis 2
Comparison groups	Exemestane (E) v Abiraterone Acetate plus Prednisone plus Exemestane (AAPE)
Number of subjects included in analysis	129
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.137
Method	Chi-squared
Parameter estimate	Risk ratio (RR)
Point estimate	1.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.816
upper limit	3.926

Statistical analysis title	Statistical Analysis 1
Comparison groups	Exemestane (E) v Abiraterone Acetate plus Prednisone (AAP)
Number of subjects included in analysis	115
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.603
Method	Chi-squared
Parameter estimate	Risk ratio (RR)
Point estimate	0.757
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.264
upper limit	2.175

Secondary: Change from Baseline in Serum Endocrine Biomarkers (Estradiol and Estrone) at End of Treatment

End point title	Change from Baseline in Serum Endocrine Biomarkers (Estradiol and Estrone) at End of Treatment
End point description: Change from baseline in serum endocrine biomarkers (estradiol and estrone) was summarized by treatment at end of treatment. ITT analysis set with valid baseline value and at least 1 post baseline value. Here "n" (number of subjects analyzed)" signifies subjects evaluable for specified categories, for each arm respectively.	
End point type	Secondary
End point timeframe: Baseline and End of treatment (approximately 2 years)	

End point values	Exemestane (E)	Abiraterone Acetate plus Prednisone (AAP)	Abiraterone Acetate plus Prednisone plus Exemestane (AAPE)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	102	89	106	
Units: Picomoles Per Liter (Pmol/L)				
arithmetic mean (standard deviation)				
Estradiol (n=50, 49, 56)	1.53 (± 27.643)	-3.35 (± 13.634)	-1.04 (± 20.146)	
Estrone (n=46, 49, 56)	-34.20 (± 83.770)	-28.09 (± 47.779)	-30.60 (± 42.385)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Serum Endocrine Biomarkers (Progesterone and Testosterone) at End of Treatment

End point title	Change from Baseline in Serum Endocrine Biomarkers (Progesterone and Testosterone) at End of Treatment
End point description: Change from baseline in serum endocrine biomarkers (Progesterone and Testosterone) was summarized by treatment at end of treatment. ITT analysis set with valid baseline value and at least 1 post baseline value. Here "n" (number of subjects analyzed)" signifies subjects evaluable for specified categories, for each arm respectively.	
End point type	Secondary
End point timeframe: Baseline and End of treatment (approximately 2 years)	

End point values	Exemestane (E)	Abiraterone Acetate plus Prednisone (AAP)	Abiraterone Acetate plus Prednisone plus Exemestane (AAPE)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	102	89	106	
Units: Nanomoles Per Liter (nmol/L)				
arithmetic mean (standard deviation)				
Progesterone (n=15, 8, 15)	-4.80 (± 18.268)	8.98 (± 15.113)	12.34 (± 16.967)	
Testosterone (n=53, 50, 56)	-0.09 (± 0.416)	-0.51 (± 0.459)	-0.48 (± 0.323)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Approximately 3 years

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	16.0
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Reporting groups

Reporting group title	Exemestane
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Reporting group description:

Subjects received exemestane tablet as oral dose of 25 milligram (mg) once daily in 28-day treatment cycles until disease progression, unacceptable toxicity, or death (up to 3 years).

Reporting group title	Abiraterone Acetate + Exemestane
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Reporting group description:

Subjects received abiraterone acetate tablet at a total oral dose of 1000 mg and 5 mg capsule of prednisone/prednisolone along with exemestane tablet 25 mg once daily in 28-day treatment cycles until disease progression, unacceptable toxicity, or death (up to 3 years).

Reporting group title	Abiraterone Acetate
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Reporting group description:

Subjects received abiraterone acetate tablet at a total oral dose of 1000 milligram (mg) along with 5 mg capsule of prednisone/prednisolone once daily in 28-day treatment cycles until disease progression, unacceptable toxicity, or death (up to 3 years).

Serious adverse events	Exemestane	Abiraterone Acetate + Exemestane	Abiraterone Acetate
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 102 (11.76%)	28 / 104 (26.92%)	18 / 87 (20.69%)
number of deaths (all causes)	20	28	24
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to Bone			
subjects affected / exposed	0 / 102 (0.00%)	1 / 104 (0.96%)	0 / 87 (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
Metastases to Peripheral Nervous System			
subjects affected / exposed	0 / 102 (0.00%)	1 / 104 (0.96%)	0 / 87 (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
Metastases to Pleura			

subjects affected / exposed	0 / 102 (0.00%)	1 / 104 (0.96%)	0 / 87 (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
Vascular disorders			
Peripheral Artery Stenosis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 104 (0.96%)	0 / 87 (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
Thrombosis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 104 (0.96%)	0 / 87 (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
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 102 (0.00%)	1 / 104 (0.96%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 102 (0.00%)	1 / 104 (0.96%)	0 / 87 (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
Malaise			
subjects affected / exposed	0 / 102 (0.00%)	1 / 104 (0.96%)	0 / 87 (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
Non-Cardiac Chest Pain			
subjects affected / exposed	1 / 102 (0.98%)	1 / 104 (0.96%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Chronic Obstructive Pulmonary Disease			

subjects affected / exposed	0 / 102 (0.00%)	1 / 104 (0.96%)	0 / 87 (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
Dysphonia			
subjects affected / exposed	0 / 102 (0.00%)	0 / 104 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	1 / 102 (0.98%)	3 / 104 (2.88%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 102 (0.00%)	1 / 104 (0.96%)	0 / 87 (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
Pleural Effusion			
subjects affected / exposed	1 / 102 (0.98%)	2 / 104 (1.92%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary Toxicity			
subjects affected / exposed	0 / 102 (0.00%)	0 / 104 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Confusional State			
subjects affected / exposed	0 / 102 (0.00%)	0 / 104 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Delirium			
subjects affected / exposed	0 / 102 (0.00%)	1 / 104 (0.96%)	0 / 87 (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
Investigations			

Aspartate Aminotransferase Increased			
subjects affected / exposed	0 / 102 (0.00%)	1 / 104 (0.96%)	0 / 87 (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
Injury, poisoning and procedural complications			
Compression Fracture			
subjects affected / exposed	0 / 102 (0.00%)	1 / 104 (0.96%)	0 / 87 (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	0 / 102 (0.00%)	0 / 104 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower Limb Fracture			
subjects affected / exposed	1 / 102 (0.98%)	0 / 104 (0.00%)	0 / 87 (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
Cardiac disorders			
Atrial Fibrillation			
subjects affected / exposed	0 / 102 (0.00%)	1 / 104 (0.96%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac Failure Congestive			
subjects affected / exposed	0 / 102 (0.00%)	1 / 104 (0.96%)	0 / 87 (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
Nervous system disorders			
Balance Disorder			
subjects affected / exposed	1 / 102 (0.98%)	0 / 104 (0.00%)	0 / 87 (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
Sciatica			

subjects affected / exposed	1 / 102 (0.98%)	0 / 104 (0.00%)	0 / 87 (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 Encephalopathy			
subjects affected / exposed	0 / 102 (0.00%)	1 / 104 (0.96%)	0 / 87 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 102 (0.00%)	1 / 104 (0.96%)	0 / 87 (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
Febrile Neutropenia			
subjects affected / exposed	0 / 102 (0.00%)	1 / 104 (0.96%)	0 / 87 (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
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 102 (0.98%)	0 / 104 (0.00%)	0 / 87 (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 disorders			
Abdominal Pain			
subjects affected / exposed	0 / 102 (0.00%)	3 / 104 (2.88%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anorectal Varices			
subjects affected / exposed	0 / 102 (0.00%)	1 / 104 (0.96%)	0 / 87 (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
Ascites			
subjects affected / exposed	0 / 102 (0.00%)	1 / 104 (0.96%)	0 / 87 (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

Crohn's Disease			
subjects affected / exposed	0 / 102 (0.00%)	0 / 104 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Faecal Incontinence			
subjects affected / exposed	0 / 102 (0.00%)	0 / 104 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small Intestinal Obstruction			
subjects affected / exposed	0 / 102 (0.00%)	0 / 104 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Volvulus of Small Bowel			
subjects affected / exposed	1 / 102 (0.98%)	0 / 104 (0.00%)	0 / 87 (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	0 / 102 (0.00%)	3 / 104 (2.88%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatitis Toxic			
subjects affected / exposed	0 / 102 (0.00%)	1 / 104 (0.96%)	0 / 87 (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
Hyperbilirubinaemia			
subjects affected / exposed	0 / 102 (0.00%)	1 / 104 (0.96%)	0 / 87 (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
Renal and urinary disorders			
Urinary Retention			
subjects affected / exposed	0 / 102 (0.00%)	1 / 104 (0.96%)	0 / 87 (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

Endocrine disorders			
Hypoadosteronism			
subjects affected / exposed	0 / 102 (0.00%)	1 / 104 (0.96%)	0 / 87 (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
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 102 (0.98%)	0 / 104 (0.00%)	0 / 87 (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
Back Pain			
subjects affected / exposed	0 / 102 (0.00%)	0 / 104 (0.00%)	2 / 87 (2.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone Pain			
subjects affected / exposed	0 / 102 (0.00%)	0 / 104 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Flank Pain			
subjects affected / exposed	0 / 102 (0.00%)	1 / 104 (0.96%)	0 / 87 (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
Intervertebral Disc Protrusion			
subjects affected / exposed	0 / 102 (0.00%)	0 / 104 (0.00%)	2 / 87 (2.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mobility Decreased			
subjects affected / exposed	0 / 102 (0.00%)	0 / 104 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myalgia			
subjects affected / exposed	0 / 102 (0.00%)	1 / 104 (0.96%)	0 / 87 (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

Pain in Extremity			
subjects affected / exposed	1 / 102 (0.98%)	0 / 104 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pathological Fracture			
subjects affected / exposed	0 / 102 (0.00%)	0 / 104 (0.00%)	2 / 87 (2.30%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Synovial Cyst			
subjects affected / exposed	0 / 102 (0.00%)	0 / 104 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 104 (0.96%)	0 / 87 (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
Bronchopneumonia			
subjects affected / exposed	0 / 102 (0.00%)	1 / 104 (0.96%)	0 / 87 (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
Cellulitis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 104 (0.96%)	0 / 87 (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
Device Related Infection			
subjects affected / exposed	0 / 102 (0.00%)	1 / 104 (0.96%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 104 (0.96%)	0 / 87 (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
Respiratory Tract Infection			

subjects affected / exposed	1 / 102 (0.98%)	0 / 104 (0.00%)	0 / 87 (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
Urinary Tract Infection			
subjects affected / exposed	0 / 102 (0.00%)	0 / 104 (0.00%)	1 / 87 (1.15%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	1 / 102 (0.98%)	1 / 104 (0.96%)	0 / 87 (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
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	0 / 102 (0.00%)	1 / 104 (0.96%)	0 / 87 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	1 / 102 (0.98%)	0 / 104 (0.00%)	3 / 87 (3.45%)
occurrences causally related to treatment / all	0 / 1	0 / 0	4 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Exemestane	Abiraterone Acetate + Exemestane	Abiraterone Acetate
Total subjects affected by non-serious adverse events			
subjects affected / exposed	79 / 102 (77.45%)	84 / 104 (80.77%)	76 / 87 (87.36%)
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	7 / 102 (6.86%)	11 / 104 (10.58%)	5 / 87 (5.75%)
occurrences (all)	11	17	9
Aspartate Aminotransferase Increased			
subjects affected / exposed	8 / 102 (7.84%)	14 / 104 (13.46%)	5 / 87 (5.75%)
occurrences (all)	12	21	6
Weight Decreased			

subjects affected / exposed occurrences (all)	4 / 102 (3.92%) 4	8 / 104 (7.69%) 12	1 / 87 (1.15%) 1
Vascular disorders			
Hot Flush			
subjects affected / exposed	14 / 102 (13.73%)	9 / 104 (8.65%)	14 / 87 (16.09%)
occurrences (all)	15	9	14
Hypertension			
subjects affected / exposed	10 / 102 (9.80%)	15 / 104 (14.42%)	7 / 87 (8.05%)
occurrences (all)	15	25	13
Nervous system disorders			
Dizziness			
subjects affected / exposed	7 / 102 (6.86%)	8 / 104 (7.69%)	4 / 87 (4.60%)
occurrences (all)	9	8	4
Dysgeusia			
subjects affected / exposed	2 / 102 (1.96%)	1 / 104 (0.96%)	5 / 87 (5.75%)
occurrences (all)	2	1	5
Headache			
subjects affected / exposed	10 / 102 (9.80%)	15 / 104 (14.42%)	6 / 87 (6.90%)
occurrences (all)	12	25	7
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	7 / 102 (6.86%)	9 / 104 (8.65%)	6 / 87 (6.90%)
occurrences (all)	8	10	7
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	12 / 102 (11.76%)	9 / 104 (8.65%)	5 / 87 (5.75%)
occurrences (all)	14	19	7
Fatigue			
subjects affected / exposed	27 / 102 (26.47%)	21 / 104 (20.19%)	24 / 87 (27.59%)
occurrences (all)	35	36	31
Influenza Like Illness			
subjects affected / exposed	7 / 102 (6.86%)	2 / 104 (1.92%)	0 / 87 (0.00%)
occurrences (all)	7	2	0
Oedema Peripheral			
subjects affected / exposed	7 / 102 (6.86%)	10 / 104 (9.62%)	6 / 87 (6.90%)
occurrences (all)	8	12	9

Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	7 / 102 (6.86%)	14 / 104 (13.46%)	4 / 87 (4.60%)
occurrences (all)	7	19	5
Constipation			
subjects affected / exposed	9 / 102 (8.82%)	15 / 104 (14.42%)	14 / 87 (16.09%)
occurrences (all)	9	19	15
Diarrhoea			
subjects affected / exposed	9 / 102 (8.82%)	13 / 104 (12.50%)	5 / 87 (5.75%)
occurrences (all)	10	27	6
Dyspepsia			
subjects affected / exposed	3 / 102 (2.94%)	6 / 104 (5.77%)	5 / 87 (5.75%)
occurrences (all)	3	11	5
Nausea			
subjects affected / exposed	18 / 102 (17.65%)	22 / 104 (21.15%)	21 / 87 (24.14%)
occurrences (all)	21	28	26
Vomiting			
subjects affected / exposed	7 / 102 (6.86%)	19 / 104 (18.27%)	12 / 87 (13.79%)
occurrences (all)	8	24	14
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	4 / 102 (3.92%)	12 / 104 (11.54%)	9 / 87 (10.34%)
occurrences (all)	7	13	10
Dyspnoea			
subjects affected / exposed	8 / 102 (7.84%)	14 / 104 (13.46%)	6 / 87 (6.90%)
occurrences (all)	8	19	6
Oropharyngeal Pain			
subjects affected / exposed	0 / 102 (0.00%)	3 / 104 (2.88%)	6 / 87 (6.90%)
occurrences (all)	0	3	6
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	2 / 102 (1.96%)	6 / 104 (5.77%)	1 / 87 (1.15%)
occurrences (all)	2	7	1
Psychiatric disorders			
Insomnia			

subjects affected / exposed occurrences (all)	9 / 102 (8.82%) 9	5 / 104 (4.81%) 6	4 / 87 (4.60%) 5
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	17 / 102 (16.67%)	11 / 104 (10.58%)	8 / 87 (9.20%)
occurrences (all)	24	14	10
Back Pain			
subjects affected / exposed	12 / 102 (11.76%)	17 / 104 (16.35%)	15 / 87 (17.24%)
occurrences (all)	19	23	20
Bone Pain			
subjects affected / exposed	18 / 102 (17.65%)	13 / 104 (12.50%)	13 / 87 (14.94%)
occurrences (all)	26	20	19
Muscle Spasms			
subjects affected / exposed	2 / 102 (1.96%)	7 / 104 (6.73%)	5 / 87 (5.75%)
occurrences (all)	2	8	6
Musculoskeletal Pain			
subjects affected / exposed	6 / 102 (5.88%)	9 / 104 (8.65%)	7 / 87 (8.05%)
occurrences (all)	7	11	7
Myalgia			
subjects affected / exposed	11 / 102 (10.78%)	5 / 104 (4.81%)	4 / 87 (4.60%)
occurrences (all)	16	5	4
Pain in Extremity			
subjects affected / exposed	7 / 102 (6.86%)	10 / 104 (9.62%)	7 / 87 (8.05%)
occurrences (all)	10	10	7
Infections and infestations			
Bronchitis			
subjects affected / exposed	4 / 102 (3.92%)	8 / 104 (7.69%)	7 / 87 (8.05%)
occurrences (all)	4	8	8
Nasopharyngitis			
subjects affected / exposed	11 / 102 (10.78%)	9 / 104 (8.65%)	5 / 87 (5.75%)
occurrences (all)	11	11	5
Urinary Tract Infection			
subjects affected / exposed	0 / 102 (0.00%)	6 / 104 (5.77%)	6 / 87 (6.90%)
occurrences (all)	0	10	8
Metabolism and nutrition disorders			

Decreased Appetite subjects affected / exposed occurrences (all)	11 / 102 (10.78%) 12	17 / 104 (16.35%) 22	13 / 87 (14.94%) 13
Hypercholesterolaemia subjects affected / exposed occurrences (all)	1 / 102 (0.98%) 1	6 / 104 (5.77%) 6	0 / 87 (0.00%) 0
Hyperglycaemia subjects affected / exposed occurrences (all)	6 / 102 (5.88%) 12	7 / 104 (6.73%) 13	3 / 87 (3.45%) 4
Hypokalaemia subjects affected / exposed occurrences (all)	4 / 102 (3.92%) 8	14 / 104 (13.46%) 28	19 / 87 (21.84%) 31

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 November 2011	The overall reason for the Amendment INT-3 was to collect circulating tumor cells (CTCs) from all subjects on study in order to improve the power of the CTC sub-study.
19 September 2012	The overall reason for the amendment INT-4 was: A prothrombin time (PT) was not done by many sites in Belgium, France, the Netherlands, and Spain, but an international normalized ratio (INR) was done instead. In addition, some subjects had abnormal but not clinically significant PT, which strictly per the current wording, would violate the protocol. This amendment allows an INR to be done whenever PT was not available. It also allows subjects with out of range PTs that were of no clinical significance to be eligible for the study.
18 March 2013	The overall reason for the Amendment INT-5 was to incorporate the recommendations of the Data Review Committee (DRC) following their review of the efficacy and safety results from the protocol specified interim analysis of progression-free survival (PFS) (110 [50 percentage] of progression or death events).
20 January 2014	The overall reason for Amendment INT-6 was about the final analysis of the primary endpoint, progression-free survival (PFS) was performed after the predefined total of 150 PFS events were reported in the abiraterone plus exemestane group and in the exemestane alone group; the clinical cutoff date for the final analysis (CCO-FA) was 20 September 2013. The results did not show a clinically meaningful or statistically significant advantage of abiraterone acetate plus exemestane or abiraterone acetate alone over exemestane alone. There was also a slight increase in the incidence of adverse events in subjects treated with abiraterone acetate or with the combination of abiraterone acetate plus exemestane versus single-agent exemestane. However, individual subjects might derive benefit from the treatment they are currently receiving with continued control of disease in the absence of significant toxicity. Therefore, it was decided to offer all subjects still on study treatment the opportunity to continue on their existing study medication for up to 2 years from the CCO-FA (ie, up to 20 September 2015), at which point the situation was reassessed for subjects still receiving study medication. Subjects who did not continue on study medication and those in long-term follow up were discontinued from the study. The decision to continue on study medication or withdraw from the study was made by the subject and the investigator.
27 April 2015	The overall reason for Amendment International (INT)-7 was to extend the period for long-term safety follow up to a maximum of 5 years from the final analysis clinical cut off.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The median overall survival (OS) was not estimable due to the high rate of censoring. Specifically for the quantitative electrocardiogram (ECG) parameters, the study was not designed for a detailed assessment of QT and corrected QT intervals.

Notes: