



## 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 |
|-----------------------|---------------|

##### 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:

| <b>Subjects enrolled per age group</b>    |     |
|-------------------------------------------|-----|
| In utero                                  | 0   |
| Preterm newborn - gestational age < 37 wk | 0   |
| Newborns (0-27 days)                      | 0   |
| Infants and toddlers (28 days-23 months)  | 0   |
| Children (2-11 years)                     | 0   |
| Adolescents (12-17 years)                 | 0   |
| Adults (18-64 years)                      | 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 [AAP 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 |
|------------------------------|-----|

|                  |                |
|------------------|----------------|
| <b>Arm title</b> | Exemestane (E) |
|------------------|----------------|

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).

|                  |                                           |
|------------------|-------------------------------------------|
| <b>Arm title</b> | Abiraterone Acetate plus Prednisone (AAP) |
|------------------|-------------------------------------------|

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).

|                  |                                                            |
|------------------|------------------------------------------------------------|
| <b>Arm title</b> | Abiraterone Acetate plus Prednisone plus Exemestane (AAPE) |
|------------------|------------------------------------------------------------|

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                                                         |
| Physician decision             | 1              | -                                         | 1                                                          |
| Consent withdrawn by subject   | 9              | 10                                        | 9                                                          |
| Other                          | 67             | 52                                        | 67                                                         |
| Lost to follow-up              | 1              | 1                                         | -                                                          |



## Baseline characteristics

### 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).

| 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<br>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<br>Units: years     |                |                                           |                                                            |
| arithmetic mean                             | 61.9           | 63.1                                      | 63.8                                                       |
| standard deviation                          | ± 8.55         | ± 9.17                                    | ± 10.91                                                    |
| Title for Gender<br>Units: subjects         |                |                                           |                                                            |
| Female                                      | 102            | 89                                        | 106                                                        |

| Reporting group values                      | Total |  |  |
|---------------------------------------------|-------|--|--|
| Number of subjects                          | 297   |  |  |
| Title for AgeCategorical<br>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<br>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:<br>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:<br>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:<br>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:<br>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:<br>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

|                                         |                                                            |
|-----------------------------------------|------------------------------------------------------------|
| <b>Statistical analysis title</b>       | 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                                                      |

|                                         |                                                                             |
|-----------------------------------------|-----------------------------------------------------------------------------|
| <b>Statistical analysis title</b>       | 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                                                                                                                                                                                                                                                                                                                                                                      |                       |

| <b>End point values</b>          | 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

| <b>Statistical analysis title</b>       | 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                                                      |

| <b>Statistical analysis title</b>       | 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

|                                         |                                                            |
|-----------------------------------------|------------------------------------------------------------|
| <b>Statistical analysis title</b>       | 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                                                      |

|                                   |                                                                             |
|-----------------------------------|-----------------------------------------------------------------------------|
| <b>Statistical analysis title</b> | 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                   |

|                                         |                                                            |
|-----------------------------------------|------------------------------------------------------------|
| <b>Statistical analysis title</b>       | 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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                       |

| <b>End point values</b>       | 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

|                                         |                                                                             |
|-----------------------------------------|-----------------------------------------------------------------------------|
| <b>Statistical analysis title</b>       | 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                                                                       |

|                                         |                                                            |
|-----------------------------------------|------------------------------------------------------------|
| <b>Statistical analysis title</b>       | 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:<br>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:<br>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:<br>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:<br>Baseline and End of treatment (approximately 2 years)                                                                                                                                                                                                                                                                                          |                                                                                                        |

| <b>End point values</b>              | 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 |
|-----------------|----------------|

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 16.0 |
|--------------------|------|

### Reporting groups

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

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 |
|-----------------------|----------------------------------|

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 |
|-----------------------|---------------------|

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 %

| <b>Non-serious adverse events</b>                     | <b>Exemestane</b> | <b>Abiraterone Acetate + Exemestane</b> | <b>Abiraterone Acetate</b> |
|-------------------------------------------------------|-------------------|-----------------------------------------|----------------------------|
| 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<br>occurrences (all)        | 4 / 102 (3.92%)<br>4 | 8 / 104 (7.69%)<br>12 | 1 / 87 (1.15%)<br>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<br>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<br>occurrences (all) | 9 / 102 (8.82%)<br>9 | 5 / 104 (4.81%)<br>6 | 4 / 87 (4.60%)<br>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<br>subjects affected / exposed<br>occurrences (all)    | 11 / 102 (10.78%)<br>12 | 17 / 104 (16.35%)<br>22 | 13 / 87 (14.94%)<br>13 |
| Hypercholesterolaemia<br>subjects affected / exposed<br>occurrences (all) | 1 / 102 (0.98%)<br>1    | 6 / 104 (5.77%)<br>6    | 0 / 87 (0.00%)<br>0    |
| Hyperglycaemia<br>subjects affected / exposed<br>occurrences (all)        | 6 / 102 (5.88%)<br>12   | 7 / 104 (6.73%)<br>13   | 3 / 87 (3.45%)<br>4    |
| Hypokalaemia<br>subjects affected / exposed<br>occurrences (all)          | 4 / 102 (3.92%)<br>8    | 14 / 104 (13.46%)<br>28 | 19 / 87 (21.84%)<br>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: