

**Clinical trial results:****A Randomized Phase 2 Study Evaluating Abiraterone Acetate With Different Steroid Regimens for Preventing Symptoms Associated With Mineralocorticoid Excess in Asymptomatic, Chemotherapy-Naive and Metastatic Castration-Resistant Prostate Cancer (mCRPC) Patients****Summary**

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2012-004331-23 |
| Trial protocol           | DE BE GB IT HU |
| Global end of trial date | 05 June 2018   |

**Results information**

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1 (current) |
| This version publication date  | 21 June 2019 |
| First version publication date | 21 June 2019 |

**Trial information****Trial identification**

|                       |          |
|-----------------------|----------|
| Sponsor protocol code | CR100916 |
|-----------------------|----------|

**Additional study identifiers**

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01867710 |
| WHO universal trial number (UTN)   | -           |

Notes:

**Sponsors**

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | Janssen-Cilag International NV   |
| Sponsor organisation address | Turnhoutseweg 30, Beerse, Belgium, 2340  |
| Public contact               | Clinical Registry Group, Janssen-Cilag International NV,<br>ClinicalTrialsEU@its.jnj.com |
| Scientific contact           | Clinical Registry Group, Janssen-Cilag International NV,<br>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                       | 05 June 2018 |
| Is this the analysis of the primary completion data? | No           |
| Global end of trial reached?                         | Yes          |
| Global end of trial date                             | 05 June 2018 |
| Was the trial ended prematurely?                     | No           |

Notes:

## General information about the trial

Main objective of the trial:

The main objective of this study was to evaluate the safety of abiraterone acetate with 4 alternative steroid treatment strategies related to symptoms associated with mineralocorticoid excess toxicities (i.e, hypokalemia and/or hypertension) during the first 24 weeks of treatment in asymptomatic, chemotherapy-naive, mCRPC (metastatic castration-resistant prostate cancer) subjects.

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 evaluations included adverse events (AEs), clinical laboratory tests (insulin resistance, lipids, ACTH [adrenocorticotrophic hormone], serum androgens, urinary steroid excretion, hematology, and serum chemistry, urinalysis), vital sign measurements, dual-energy x-ray absorptiometry (DXA) scans, physical examinations.

Background therapy: -

Evidence for comparator: -

|   |              |
|---|--------------|
| Actual start date of recruitment                          | 28 June 2013 |
| 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: 41        |
| Country: Number of subjects enrolled | Germany: 28        |
| Country: Number of subjects enrolled | United Kingdom: 35 |
| Country: Number of subjects enrolled | Hungary: 20        |
| Country: Number of subjects enrolled | Italy: 40          |
| Worldwide total number of subjects   | 164                |
| EEA total number of subjects         | 164                |

Notes:

### Subjects enrolled per age group

|   |   |
|---|---|
| In utero                                  | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days)                      | 0 |
| Infants and toddlers (28 days-23          | 0 |

|                           |     |
|---------------------------|-----|
| months)                   |     |
| Children (2-11 years)     | 0   |
| Adolescents (12-17 years) | 0   |
| Adults (18-64 years)      | 40  |
| From 65 to 84 years       | 118 |
| 85 years and over         | 6   |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Of the 204 subjects who were enrolled, 39 were screen failures and 1 subject withdrew consent before randomization. A total of 164 subjects were randomized to prednisone 5 milligram (mg) BID (41 subjects), prednisone 5 mg QD (41 subjects), prednisone 2.5 mg BID (40 subjects), and dexamethasone 0.5 mg (42 subjects) QD groups.

### 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>             | Abiraterone Acetate 1000 mg QD + Prednisone 5 mg BID |

Arm description:

Subjects received abiraterone acetate 1000 milligram (mg) tablet orally once daily (QD) and prednisone 5 mg tablet orally twice daily (BID) up to 156 Weeks. Subjects who were progression-free at 156 weeks entered the extension phase of the study and received study treatment until death, radiographic disease progression and/or unequivocal clinical progression, and/or other specific reasons for discontinuation. Subjects who ended the extension phase prematurely and subjects who did not enter the extension phase entered a follow-up phase until end of study.

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

Dosage and administration details:

Subjects received abiraterone acetate 1000 mg QD up to 156 weeks. Subjects who were progression-free at 156 weeks entered the extension phase of the study and received study treatment until death, radiographic disease progression and/or unequivocal clinical progression, and/or other specific reasons for discontinuation.

|  |            |
|--|------------|
| Investigational medicinal product name | Prednisone |
| Investigational medicinal product code |            |
| Other name                             |            |
| Pharmaceutical forms                   | Tablet     |
| Routes of administration               | Oral use   |

Dosage and administration details:

Subjects received prednisone 5 mg BID up to 156 weeks. Subjects who were progression-free at 156 weeks entered the extension phase of the study and received study treatment until death, radiographic disease progression and/or unequivocal clinical progression, and/or other specific reasons for discontinuation.

|                  |   |
|------------------|---|
| <b>Arm title</b> | Abiraterone Acetate 1000 mg QD + Prednisone 5 mg QD |
|------------------|---|

Arm description:

Subjects received abiraterone acetate 1000 mg and prednisone 5 mg tablet orally QD up to 156 Weeks. Subjects who were progression-free at 156 weeks entered the extension phase of the study and received study treatment until death, radiographic disease progression and/or unequivocal clinical progression, and/or other specific reasons for discontinuation. Subjects who ended the extension phase prematurely and subjects who did not enter the extension phase entered a follow-up phase until end of study.

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

Dosage and administration details:

Subjects received abiraterone acetate 1000 mg QD up to 156 weeks. Subjects who were progression-free at 156 weeks entered the extension phase of the study and received study treatment until death, radiographic disease progression and/or unequivocal clinical progression, and/or other specific reasons for discontinuation.

|  |            |
|--|------------|
| Investigational medicinal product name | Prednisone |
| Investigational medicinal product code |            |
| Other name                             |            |
| Pharmaceutical forms                   | Tablet     |
| Routes of administration               | Oral use   |

Dosage and administration details:

Subjects received prednisone 5 mg QD up to 156 weeks. Subjects who were progression-free at 156 weeks entered the extension phase of the study and received study treatment until death, radiographic disease progression and/or unequivocal clinical progression, and/or other specific reasons for discontinuation.

|                  |  |
|------------------|--|
| <b>Arm title</b> | Abiraterone Acetate 1000 mg QD + Prednisone 2.5 mg BID |
|------------------|--|

Arm description:

Subjects received abiraterone acetate 1000 mg tablet orally QD and prednisone 2.5 mg tablet orally BID up to 156 Weeks. Subjects who were progression-free at 156 weeks entered the extension phase of the study and received study treatment until death, radiographic disease progression and/or unequivocal clinical progression, and/or other specific reasons for discontinuation. Subjects who ended the extension phase prematurely and subjects who did not enter the extension phase entered a follow-up phase until end of study.

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

Dosage and administration details:

Subjects received prednisone 2.5 mg BID up to 156 weeks. Subjects who were progression-free at 156 weeks entered the extension phase of the study and received study treatment until death, radiographic disease progression and/or unequivocal clinical progression, and/or other specific reasons for discontinuation.

|  |                     |
|--|---------------------|
| Investigational medicinal product name | Abiraterone Acetate |
| Investigational medicinal product code |                     |
| Other name                             |                     |
| Pharmaceutical forms                   | Tablet              |
| Routes of administration               | Oral use            |

Dosage and administration details:

Subjects received abiraterone acetate 1000 mg QD up to 156 weeks. Subjects who were progression-free at 156 weeks entered the extension phase of the study and received study treatment until death, radiographic disease progression and/or unequivocal clinical progression, and/or other specific reasons for discontinuation.

|                  |  |
|------------------|--|
| <b>Arm title</b> | Abiraterone Acetate 1000 mg QD + Dexamethasone 0.5 mg QD |
|------------------|--|

Arm description:

Subjects received abiraterone acetate 1000 mg and dexamethasone 0.5 mg tablet orally QD up to 156 Weeks. Subjects who were progression-free at 156 weeks entered the extension phase of the study and received study treatment until death, radiographic disease progression and/or unequivocal clinical progression, and/or other specific reasons for discontinuation. Subjects who ended the extension phase prematurely and subjects who did not enter the extension phase entered a follow-up phase until end of

study.

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

Dosage and administration details:

Subjects received dexamethasone 0.5 mg QD up to 156 weeks. Subjects who were progression-free at 156 weeks entered the extension phase of the study and received study treatment until death, radiographic disease progression and/or unequivocal clinical progression, and/or other specific reasons for discontinuation.

|  |                     |
|--|---------------------|
| Investigational medicinal product name | Abiraterone Acetate |
| Investigational medicinal product code |                     |
| Other name                             |                     |
| Pharmaceutical forms                   | Tablet              |
| Routes of administration               | Oral use            |

Dosage and administration details:

Subjects received abiraterone acetate 1000 mg QD up to 156 weeks. Subjects who were progression-free at 156 weeks entered the extension phase of the study and received study treatment until death, radiographic disease progression and/or unequivocal clinical progression, and/or other specific reasons for discontinuation.

| Number of subjects in period 1         | Abiraterone Acetate<br>1000 mg QD +<br>Prednisone 5 mg<br>BID | Abiraterone Acetate<br>1000 mg QD +<br>Prednisone 5 mg QD | Abiraterone Acetate<br>1000 mg QD +<br>Prednisone 2.5 mg<br>BID |
|--|---|---|---|
|  | Started   | 41  | 41  |
| Treated                                | 41  | 41  | 39  |
| Completed                              | 0   | 0   | 0   |
| Not completed                          | 41  | 41  | 40  |
| Clinical progression                   | -   | -   | 1   |
| Disease progression                    | 1   | -   | -   |
| Study terminated by sponsor            | 9   | 13  | 8   |
| Patient to follow subsequent treatment | -   | 1   | -   |
| Consent withdrawn by subject           | 2   | 5   | 1   |
| Patient decision                       | -   | -   | -   |
| Death                                  | 25  | 15  | 27  |
| Study medication no longer effective   | -   | 1   | -   |
| PSA-progression                        | -   | 1   | -   |
| Progressive disease                    | 1   | -   | -   |
| Lost to follow-up                      | 3   | 4   | 3   |
| Biochemical progression                | -   | 1   | -   |
| Protocol deviation                     | -   | -   | -   |

| <b>Number of subjects in period 1</b>     | Abiraterone Acetate<br>1000 mg QD +<br>Dexamethasone 0.5<br>mg QD |
|---|---|
| Started                                   | 42  |
| Treated                                   | 42  |
| Completed                                 | 0   |
| Not completed                             | 42  |
| Clinical progression                      | -   |
| Disease progression                       | -   |
| Study terminated by sponsor               | 16  |
| Patient to follow subsequent<br>treatment | -   |
| Consent withdrawn by subject              | 2   |
| Patient decision                          | 1   |
| Death                                     | 20  |
| Study medication no longer<br>effective   | -   |
| PSA-progression                           | -   |
| Progressive disease                       | -   |
| Lost to follow-up                         | 2   |
| Biochemical progression                   | -   |
| Protocol deviation                        | 1   |

## Baseline characteristics

### Reporting groups

|                       |  |
|-----------------------|--|
| Reporting group title | Abiraterone Acetate 1000 mg QD + Prednisone 5 mg BID |
|-----------------------|--|

Reporting group description:

Subjects received abiraterone acetate 1000 milligram (mg) tablet orally once daily (QD) and prednisone 5 mg tablet orally twice daily (BID) up to 156 Weeks. Subjects who were progression-free at 156 weeks entered the extension phase of the study and received study treatment until death, radiographic disease progression and/or unequivocal clinical progression, and/or other specific reasons for discontinuation. Subjects who ended the extension phase prematurely and subjects who did not enter the extension phase entered a follow-up phase until end of study.

|                       |   |
|-----------------------|---|
| Reporting group title | Abiraterone Acetate 1000 mg QD + Prednisone 5 mg QD |
|-----------------------|---|

Reporting group description:

Subjects received abiraterone acetate 1000 mg and prednisone 5 mg tablet orally QD up to 156 Weeks. Subjects who were progression-free at 156 weeks entered the extension phase of the study and received study treatment until death, radiographic disease progression and/or unequivocal clinical progression, and/or other specific reasons for discontinuation. Subjects who ended the extension phase prematurely and subjects who did not enter the extension phase entered a follow-up phase until end of study.

|                       |  |
|-----------------------|--|
| Reporting group title | Abiraterone Acetate 1000 mg QD + Prednisone 2.5 mg BID |
|-----------------------|--|

Reporting group description:

Subjects received abiraterone acetate 1000 mg tablet orally QD and prednisone 2.5 mg tablet orally BID up to 156 Weeks. Subjects who were progression-free at 156 weeks entered the extension phase of the study and received study treatment until death, radiographic disease progression and/or unequivocal clinical progression, and/or other specific reasons for discontinuation. Subjects who ended the extension phase prematurely and subjects who did not enter the extension phase entered a follow-up phase until end of study.

|                       |  |
|-----------------------|--|
| Reporting group title | Abiraterone Acetate 1000 mg QD + Dexamethasone 0.5 mg QD |
|-----------------------|--|

Reporting group description:

Subjects received abiraterone acetate 1000 mg and dexamethasone 0.5 mg tablet orally QD up to 156 Weeks. Subjects who were progression-free at 156 weeks entered the extension phase of the study and received study treatment until death, radiographic disease progression and/or unequivocal clinical progression, and/or other specific reasons for discontinuation. Subjects who ended the extension phase prematurely and subjects who did not enter the extension phase entered a follow-up phase until end of study.

| Reporting group values                      | Abiraterone Acetate 1000 mg QD + Prednisone 5 mg BID | Abiraterone Acetate 1000 mg QD + Prednisone 5 mg QD | Abiraterone Acetate 1000 mg QD + Prednisone 2.5 mg BID |
|---|--|---|--|
| Number of subjects                          | 41   | 41  | 40   |
| Title for AgeCategorical<br>Units: subjects |  |   |  |
| Children (2-11 years)                       | 0  | 0   | 0  |
| Adolescents (12-17 years)                   | 0  | 0   | 0  |
| Adults (18-64 years)                        | 12   | 12  | 8  |
| From 65 to 84 years                         | 26   | 28  | 32   |
| 85 years and over                           | 3  | 1   | 0  |
| Title for AgeContinuous<br>Units: years     |  |   |  |
| arithmetic mean                             | 68.9   | 69  | 69.3   |
| standard deviation                          | ± 9.28   | ± 8.44  | ± 7.51   |
| Title for Gender<br>Units: subjects         |  |   |  |
| Male  | 41   | 41  | 40   |

| <b>Reporting group values</b>               | Abiraterone Acetate<br>1000 mg QD +<br>Dexamethasone 0.5<br>mg QD | Total |  |
|---|---|-------|--|
| Number of subjects                          | 42  | 164   |  |
| Title for AgeCategorical<br>Units: subjects |   |       |  |
| Children (2-11 years)                       | 0   | 0     |  |
| Adolescents (12-17 years)                   | 0   | 0     |  |
| Adults (18-64 years)                        | 8   | 40    |  |
| From 65 to 84 years                         | 32  | 118   |  |
| 85 years and over                           | 2   | 6     |  |
| Title for AgeContinuous<br>Units: years     |   |       |  |
| arithmetic mean                             | 71.3  |       |  |
| standard deviation                          | ± 8.12  | -     |  |
| Title for Gender<br>Units: subjects         |   |       |  |
| Male  | 42  | 164   |  |

## End points

### End points reporting groups

|                       |  |
|-----------------------|--|
| Reporting group title | Abiraterone Acetate 1000 mg QD + Prednisone 5 mg BID |
|-----------------------|--|

Reporting group description:

Subjects received abiraterone acetate 1000 milligram (mg) tablet orally once daily (QD) and prednisone 5 mg tablet orally twice daily (BID) up to 156 Weeks. Subjects who were progression-free at 156 weeks entered the extension phase of the study and received study treatment until death, radiographic disease progression and/or unequivocal clinical progression, and/or other specific reasons for discontinuation. Subjects who ended the extension phase prematurely and subjects who did not enter the extension phase entered a follow-up phase until end of study.

|                       |   |
|-----------------------|---|
| Reporting group title | Abiraterone Acetate 1000 mg QD + Prednisone 5 mg QD |
|-----------------------|---|

Reporting group description:

Subjects received abiraterone acetate 1000 mg and prednisone 5 mg tablet orally QD up to 156 Weeks. Subjects who were progression-free at 156 weeks entered the extension phase of the study and received study treatment until death, radiographic disease progression and/or unequivocal clinical progression, and/or other specific reasons for discontinuation. Subjects who ended the extension phase prematurely and subjects who did not enter the extension phase entered a follow-up phase until end of study.

|                       |  |
|-----------------------|--|
| Reporting group title | Abiraterone Acetate 1000 mg QD + Prednisone 2.5 mg BID |
|-----------------------|--|

Reporting group description:

Subjects received abiraterone acetate 1000 mg tablet orally QD and prednisone 2.5 mg tablet orally BID up to 156 Weeks. Subjects who were progression-free at 156 weeks entered the extension phase of the study and received study treatment until death, radiographic disease progression and/or unequivocal clinical progression, and/or other specific reasons for discontinuation. Subjects who ended the extension phase prematurely and subjects who did not enter the extension phase entered a follow-up phase until end of study.

|                       |  |
|-----------------------|--|
| Reporting group title | Abiraterone Acetate 1000 mg QD + Dexamethasone 0.5 mg QD |
|-----------------------|--|

Reporting group description:

Subjects received abiraterone acetate 1000 mg and dexamethasone 0.5 mg tablet orally QD up to 156 Weeks. Subjects who were progression-free at 156 weeks entered the extension phase of the study and received study treatment until death, radiographic disease progression and/or unequivocal clinical progression, and/or other specific reasons for discontinuation. Subjects who ended the extension phase prematurely and subjects who did not enter the extension phase entered a follow-up phase until end of study.

### Primary: Percentage of Subjects Experiencing Neither of the 2 Mineralocorticoid Excess Toxicity During the First 24 Weeks of Treatment

|                 |  |
|-----------------|--|
| End point title | Percentage of Subjects Experiencing Neither of the 2 Mineralocorticoid Excess Toxicity During the First 24 Weeks of Treatment <sup>[1]</sup> |
|-----------------|--|

End point description:

No mineralocorticoid excess is defined as experiencing neither of the 2 mineralocorticoid excess toxicities, that is, neither hypokalemia nor hypertension. Safety population included all randomized and treated subjects. Here "N" (Number of subjects analyzed) signifies those subjects who were evaluable for this endpoint.

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

End point timeframe:

Week 24

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Descriptive statistics were done, no inferential statistical analyses were performed.

| <b>End point values</b>          | Abiraterone Acetate 1000 mg QD + Prednisone 5 mg BID | Abiraterone Acetate 1000 mg QD + Prednisone 5 mg QD | Abiraterone Acetate 1000 mg QD + Prednisone 2.5 mg BID | Abiraterone Acetate 1000 mg QD + Dexamethasone 0.5 mg QD |
|----------------------------------|--|---|--|--|
| Subject group type               | Reporting group                                      | Reporting group                                     | Reporting group  | Reporting group  |
| Number of subjects analysed      | 34   | 38  | 35   | 37   |
| Units: Percentage of subjects    |  |   |  |  |
| number (confidence interval 95%) |  |   |  |  |
| Percentage of subjects           | 70.6 (53.8 to 83.2)                                  | 36.8 (23.4 to 52.7)                                 | 60.0 (43.6 to 74.4)                                    | 70.3 (54.2 to 82.5)                                      |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of Subjects With Confirmed Prostate Specific Antigen (PSA) Response Rate [Greater Than or Equal to (>=) 50 Percent (%) Decline From Baseline] at Week 12

|                 |   |
|-----------------|---|
| End point title | Percentage of Subjects With Confirmed Prostate Specific Antigen (PSA) Response Rate [Greater Than or Equal to (>=) 50 Percent (%) Decline From Baseline] at Week 12 |
|-----------------|---|

End point description:

The PSA response is defined as a  $\geq 50\%$  decline from baseline according to the adapted Prostate Cancer Working Group 2 (PCWG2) criteria. For a PSA response to be confirmed, an additional PSA measurement obtained 4 or more weeks later has to show  $\geq 50\%$  decline from baseline. Intent-to-treat (ITT) population included all randomized subjects regardless of whether they received any study treatment. Here "N" (Number of subjects analyzed) signifies those subjects who were evaluable for this endpoint.

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

End point timeframe:

Week 12

| <b>End point values</b>          | Abiraterone Acetate 1000 mg QD + Prednisone 5 mg BID | Abiraterone Acetate 1000 mg QD + Prednisone 5 mg QD | Abiraterone Acetate 1000 mg QD + Prednisone 2.5 mg BID | Abiraterone Acetate 1000 mg QD + Dexamethasone 0.5 mg QD |
|----------------------------------|--|---|--|--|
| Subject group type               | Reporting group                                      | Reporting group                                     | Reporting group  | Reporting group  |
| Number of subjects analysed      | 35   | 34  | 36   | 39   |
| Units: Percentage of subjects    |  |   |  |  |
| number (confidence interval 95%) | 57.1 (39.4 to 73.7)                                  | 70.6 (52.5 to 84.9)                                 | 47.2 (30.4 to 64.5)                                    | 79.5 (63.5 to 90.7)                                      |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline to Endpoint in Brief Pain Inventory- Short Form

**(BPI-SF) Score: Worst Pain**

|                 |  |
|-----------------|--|
| End point title | Change From Baseline to Endpoint in Brief Pain Inventory-Short Form (BPI-SF) Score: Worst Pain |
|-----------------|--|

## End point description:

BPI-SF is 11-item self-reported questionnaire designed to assess severity and impact of pain on daily functions (pain interference). It includes 4 questions that assess pain intensity/severity (worst, least, average, right now) and 7 questions that assess impact of pain on daily functions (general activity, mood, walking ability, normal work, relations with other people, sleep, enjoyment of life). BPI-SF scores range from 0=No pain to 10=Pain as bad as you can imagine; Higher scores indicate greater pain. Worst pain item has scale of 0 to 10 with 0 indicating "No pain" and 10 indicating "Pain as bad as you can imagine". Last observation carried forward (LOCF) approach used for endpoint analysis. Last observation defined as last visit with non-missing data for parameter analyzed. ITT population included all randomized subjects regardless of whether they received any study treatment. Here "N" (Number of Subjects Analyzed) signifies those subjects who were evaluable for this endpoint.

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

## End point timeframe:

Baseline up to the Endpoint (last post-baseline assessment value during 156 weeks of main study treatment period [MSTP])

| End point values                     | Abiraterone Acetate 1000 mg QD + Prednisone 5 mg BID | Abiraterone Acetate 1000 mg QD + Prednisone 5 mg QD | Abiraterone Acetate 1000 mg QD + Prednisone 2.5 mg BID | Abiraterone Acetate 1000 mg QD + Dexamethasone 0.5 mg QD |
|--------------------------------------|--|---|--|--|
| Subject group type                   | Reporting group                                      | Reporting group                                     | Reporting group  | Reporting group  |
| Number of subjects analysed          | 36   | 33  | 37   | 38   |
| Units: Units on a scale              |  |   |  |  |
| arithmetic mean (standard deviation) | 1.6 (± 2.43)   | 2.2 (± 2.86)  | 2.5 (± 2.39)   | 1.3 (± 2.28)   |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Change From Baseline to Endpoint in Brief Pain Inventory- Short Form (BPI-SF) Score: Pain Intensity Subscale**

|                 |   |
|-----------------|---|
| End point title | Change From Baseline to Endpoint in Brief Pain Inventory-Short Form (BPI-SF) Score: Pain Intensity Subscale |
|-----------------|---|

## End point description:

BPI-SF is 11-item self-reported questionnaire designed to assess severity and impact of pain on daily functions (pain interference). It includes 4 questions that assess pain intensity/severity (worst, least, average, right now) and 7 questions that assess impact of pain on daily functions (general activity, mood, walking ability, normal work, relations with other people, sleep, enjoyment of life). BPI-SF scores range from 0=No pain to 10=Pain as bad as you can imagine; Higher scores indicate greater pain. Pain Severity Index is the mean of 4 pain scores on BPI-SF; range is 0=No pain to 10=Pain as bad as you can imagine; Higher score indicates greater pain severity. LOCF approach used for endpoint analysis. Last observation defined as last visit with non-missing data for parameter analyzed. ITT population: all randomized subjects regardless of whether they received any study treatment. 'N' (number of subjects analyzed)- number of subjects who were evaluable for this endpoint.

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

## End point timeframe:

Baseline up to the Endpoint (last post-baseline assessment value during 156 weeks of MSTP)

| <b>End point values</b>              | Abiraterone Acetate 1000 mg QD + Prednisone 5 mg BID | Abiraterone Acetate 1000 mg QD + Prednisone 5 mg QD | Abiraterone Acetate 1000 mg QD + Prednisone 2.5 mg BID | Abiraterone Acetate 1000 mg QD + Dexamethasone 0.5 mg QD |
|--------------------------------------|--|---|--|--|
| Subject group type                   | Reporting group                                      | Reporting group                                     | Reporting group  | Reporting group  |
| Number of subjects analysed          | 37   | 35  | 37   | 38   |
| Units: Units on a scale              |  |   |  |  |
| arithmetic mean (standard deviation) | 1.31 (± 1.788)                                       | 1.37 (± 1.952)                                      | 1.80 (± 2.014)   | 0.97 (± 1.610)   |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change From Baseline to Endpoint in Brief Pain Inventory- Short Form (BPI-SF) Score: Pain Interference Subscale

|                 |   |
|-----------------|---|
| End point title | Change From Baseline to Endpoint in Brief Pain Inventory- Short Form (BPI-SF) Score: Pain Interference Subscale |
|-----------------|---|

End point description:

BPI-SF is 11-item self-reported questionnaire designed to assess severity and impact of pain on daily functions (pain interference). It includes 4 questions that assess pain intensity/severity (worst, least, average, right now) and 7 questions that assess impact of pain on daily functions (general activity, mood, walking ability, normal work, relations with other people, sleep, enjoyment of life). BPI-SF scores range from 0=No pain to 10=Pain as bad as you can imagine; Higher scores indicate greater pain. Pain Interference Index is the mean of the scores for the 7 items of the BPI-SF; range is 0=Does not interfere to 10=Completely interferes. LOCF approach used for endpoint analysis. Last observation defined as last visit with non-missing data for parameter analyzed. ITT population: all randomized subjects regardless of whether they received any study treatment. 'N' (number of subjects analyzed)- number of subjects who were evaluable for this endpoint.

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

End point timeframe:

Baseline up to the Endpoint (last post-baseline assessment value during 156 weeks of MSTP)

| <b>End point values</b>              | Abiraterone Acetate 1000 mg QD + Prednisone 5 mg BID | Abiraterone Acetate 1000 mg QD + Prednisone 5 mg QD | Abiraterone Acetate 1000 mg QD + Prednisone 2.5 mg BID | Abiraterone Acetate 1000 mg QD + Dexamethasone 0.5 mg QD |
|--------------------------------------|--|---|--|--|
| Subject group type                   | Reporting group                                      | Reporting group                                     | Reporting group  | Reporting group  |
| Number of subjects analysed          | 32   | 30  | 35   | 37   |
| Units: Units on a scale              |  |   |  |  |
| arithmetic mean (standard deviation) | 0.89 (± 1.794)                                       | 1.76 (± 2.100)                                      | 1.52 (± 2.180)   | 1.12 (± 1.687)   |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline to Endpoint in EuroQol-5 Dimension-5 Level (EQ-5D-5L): Index Score

|                 |   |
|-----------------|---|
| End point title | Change From Baseline to Endpoint in EuroQol-5 Dimension-5 Level (EQ-5D-5L): Index Score |
|-----------------|---|

End point description:

EQ-5D-5L measures health outcome self-completed by respondents. It consists of EQ-5D-5L descriptive system and EQ visual analogue scale (EQ-VAS). The descriptive system comprises of 5 dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each has 5 levels (1-no problem, 2-slight problems, 3-moderate problems, 4-severe problems, 5-extreme problems). Subject selects answer for each of 5 dimensions considering response that best matches his/her health "today". Responses were used to generate a Health Status Index (HSI). HSI ranges from -0.148 to 0.949 and is anchored at 0 (health state value equal to dead) and 1 (full health). LOCF approach used for endpoint analysis. Last observation defined as last visit with non-missing data for parameter analyzed. ITT population: all randomized subjects regardless of whether they received any study treatment. 'N' (number of subjects analyzed)- number of subjects who were evaluable for this endpoint.

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

End point timeframe:

Baseline up to the Endpoint (last post-baseline assessment value during 156 weeks of MSTP)

| End point values                     | Abiraterone Acetate 1000 mg QD + Prednisone 5 mg BID | Abiraterone Acetate 1000 mg QD + Prednisone 5 mg QD | Abiraterone Acetate 1000 mg QD + Prednisone 2.5 mg BID | Abiraterone Acetate 1000 mg QD + Dexamethasone 0.5 mg QD |
|--------------------------------------|--|---|--|--|
| Subject group type                   | Reporting group                                      | Reporting group                                     | Reporting group  | Reporting group  |
| Number of subjects analysed          | 37   | 38  | 36   | 38   |
| Units: Units on a scale              |  |   |  |  |
| arithmetic mean (standard deviation) | -0.0694 ( $\pm$ 0.18402)                             | -0.0638 ( $\pm$ 0.17772)                            | -0.0728 ( $\pm$ 0.18113)                               | -0.0359 ( $\pm$ 0.13515)                                 |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline to Endpoint in EuroQol-5 Dimension-5 Level (EQ-5D-5L): EQ-VAS

|                 |  |
|-----------------|--|
| End point title | Change From Baseline to Endpoint in EuroQol-5 Dimension-5 Level (EQ-5D-5L): EQ-VAS |
|-----------------|--|

End point description:

EQ-5D-5L measures health outcome self-completed by respondents. It consists of EQ-5D-5L descriptive system and EQ visual analogue scale (EQ-VAS). EQ-VAS self-rating records the respondent's own assessment of his/her overall health status at time of completion, on scale of 0 (the worst health you can imagine) to 100 (the best health you can imagine). LOCF approach used for endpoint analysis. Last observation defined as last visit with non-missing data for parameter analyzed. ITT population: all randomized subjects regardless of whether they received any study treatment. 'N' (number of subjects analyzed)- number of subjects who were evaluable for this endpoint.

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

End point timeframe:

Baseline up to the Endpoint (last post-baseline assessment value during 156 weeks of MSTP)

| <b>End point values</b>              | Abiraterone Acetate 1000 mg QD + Prednisone 5 mg BID | Abiraterone Acetate 1000 mg QD + Prednisone 5 mg QD | Abiraterone Acetate 1000 mg QD + Prednisone 2.5 mg BID | Abiraterone Acetate 1000 mg QD + Dexamethasone 0.5 mg QD |
|--------------------------------------|--|---|--|--|
| Subject group type                   | Reporting group                                      | Reporting group                                     | Reporting group  | Reporting group  |
| Number of subjects analysed          | 38   | 37  | 37   | 37   |
| Units: Units on a scale              |  |   |  |  |
| arithmetic mean (standard deviation) | -4.5 (± 18.11)                                       | -5.0 (± 16.82)                                      | -6.6 (± 15.09)   | -3.1 (± 13.00)   |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Change From Baseline to Endpoint in Functional Assessment of Cancer Therapy-Prostate (FACT-P) Questionnaire Score

|                 |   |
|-----------------|---|
| End point title | Change From Baseline to Endpoint in Functional Assessment of Cancer Therapy-Prostate (FACT-P) Questionnaire Score |
|-----------------|---|

End point description:

FACT-P is 39-item subject rated questionnaire consists of 5 subscales assessing physical well-being (7 items; score range 0-28), social/family well-being (7 items; score range 0-28), emotional well-being (6 items; score range 0-24), functional well-being (7 items; score range 0-28), prostate-specific concerns (12 items; score range 0-48). Each item rated on 0-4 Likert type scale and combined to produce subscale scores for each domain, as well as global QoL score that ranges from 0-156. Higher scores=better QoL. Additional Concerns subscale has 12 items, each with score 0-6 making total subscale range 0-72 (higher scores are better). Missing data imputed per FACT-P Ver4 scoring system (sum of item scores\*number of items in subscale/number of items answered). Last observation defined as last visit with non-missing data for parameter. ITT population analyzed. Here 'n'(number of subjects analyzed) signifies number of subjects analyzed in specific category.

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

End point timeframe:

Baseline up to the Endpoint (last post-baseline assessment value during 156 weeks of MSTP)

| <b>End point values</b>                  | Abiraterone Acetate 1000 mg QD + Prednisone 5 mg BID | Abiraterone Acetate 1000 mg QD + Prednisone 5 mg QD | Abiraterone Acetate 1000 mg QD + Prednisone 2.5 mg BID | Abiraterone Acetate 1000 mg QD + Dexamethasone 0.5 mg QD |
|--|--|---|--|--|
| Subject group type                       | Reporting group                                      | Reporting group                                     | Reporting group  | Reporting group  |
| Number of subjects analysed              | 41   | 41  | 40   | 42   |
| Units: Units on a scale                  |  |   |  |  |
| arithmetic mean (standard deviation)     |  |   |  |  |
| Physical Well-Being(n=37,38,37,38)       | -0.98 (± 3.930)                                      | -2.20 (± 4.449)                                     | -2.46 (± 4.124)  | -1.04 (± 3.268)  |
| Social/Family Well-Being (n=37,37,36,38) | -0.01 (± 3.679)                                      | 0.61 (± 3.794)                                      | -0.78 (± 5.177)  | -1.97 (± 5.749)  |
| Emotional Well-Being (n=37,38,35,36)     | -1.46 (± 4.785)                                      | -0.89 (± 3.289)                                     | -1.66 (± 3.915)  | -0.02 (± 3.542)  |

|                                       |                  |                  |                   |                  |
|---------------------------------------|------------------|------------------|-------------------|------------------|
| Functional Well-Being (n=36,38,36,36) | -1.13 (± 4.575)  | -2.19 (± 5.767)  | -2.67 (± 5.957)   | -2.95 (± 6.698)  |
| Global Score (n=35,38,36,34)          | -4.73 (± 18.248) | -6.62 (± 17.118) | -10.39 (± 20.798) | -5.77 (± 18.322) |
| Additional Concerns (n=37,38,37,38)   | -1.29 (± 7.694)  | -2.35 (± 6.342)  | -3.96 (± 6.492)   | -0.72 (± 6.080)  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Progression-Free Survival (PFS)

|  |                                 |
|--|---------------------------------|
| End point title  | Progression-Free Survival (PFS) |
| End point description:   |                                 |
| PFS: Time from randomization to one of following: radiographic progression (RP), clinical progression (CP) or death. RP- per PCWG2 criteria and modified RECIST as time from randomization to one of following: 1) considered to have progressed by bone scan if: a) first scan with $\geq 2$ new lesions compared to baseline at $< 12$ weeks from randomization and confirmed by second scan $\geq 6$ weeks later with $\geq 2$ additional new lesions, b) first scan with $\geq 2$ new lesions compared to baseline at $\geq 12$ weeks from randomization and new lesions on next bone scan $\geq 6$ weeks later; 2) Progression of soft tissue lesions per modified RECIST; CP: cancer pain requiring initiation of chronic use of opiate or immediate need to initiate cytotoxic chemotherapy or either radiation therapy or surgical intervention for complications due to tumor progression, even in absence of RP, Or deterioration in ECOG performance status to grade 3 or above. Efficacy analysis set included ITT population. |                                 |
| End point type   | Secondary                       |
| End point timeframe:   |                                 |
| Up to 4.9 years  |                                 |

| End point values                 | Abiraterone Acetate 1000 mg QD + Prednisone 5 mg BID | Abiraterone Acetate 1000 mg QD + Prednisone 5 mg QD | Abiraterone Acetate 1000 mg QD + Prednisone 2.5 mg BID | Abiraterone Acetate 1000 mg QD + Dexamethasone 0.5 mg QD |
|----------------------------------|--|---|--|--|
| Subject group type               | Reporting group                                      | Reporting group                                     | Reporting group  | Reporting group  |
| Number of subjects analysed      | 41   | 41  | 40   | 42   |
| Units: Months                    |  |   |  |  |
| median (confidence interval 95%) | 16.16 (9.95 to 23.75)                                | 12.68 (7.66 to 29.47)                               | 8.51 (5.62 to 15.44)                                   | 21.22 (15.08 to 38.44)                                   |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Time to Prostate-Specific Antigen (PSA) Progression

|  |   |
|--|---|
| End point title  | Time to Prostate-Specific Antigen (PSA) Progression |
| End point description:   |   |
| Time to PSA progression was defined as time interval from the date of randomization to the date of the first prostate-specific antigen (PSA) progression as defined in the protocol-specific Prostate Specific Antigen Working Group 2 (PSAWG2) criteria during the main study treatment period. PCWG2 defines |   |

PSA progression as the date that a 25 percent (%) or greater increase and an absolute increase of 2 nanogram per milliliter (ng/mL) or more from the nadir is documented, which is confirmed by a second value obtained 3 or more weeks later. Efficacy analysis set included ITT population- all randomized subjects regardless of whether they received any study treatment. '99999' indicates that upper limit of 95% Confidence Interval (CI) was not estimable due to a limited number of events and the small sample size.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Up to 156 weeks      |           |

| End point values                 | Abiraterone Acetate 1000 mg QD + Prednisone 5 mg BID | Abiraterone Acetate 1000 mg QD + Prednisone 5 mg QD | Abiraterone Acetate 1000 mg QD + Prednisone 2.5 mg BID | Abiraterone Acetate 1000 mg QD + Dexamethasone 0.5 mg QD |
|----------------------------------|--|---|--|--|
| Subject group type               | Reporting group                                      | Reporting group                                     | Reporting group  | Reporting group  |
| Number of subjects analysed      | 41   | 41  | 40   | 42   |
| Units: Months                    |  |   |  |  |
| median (confidence interval 95%) | 10.38 (10.05 to 20.99)                               | 10.22 (7.39 to 26.84)                               | 4.83 (2.79 to 10.15)                                   | 18.56 (10.15 to 99999)                                   |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Objective Response Rate (ORR)

|                 |                               |
|-----------------|-------------------------------|
| End point title | Objective Response Rate (ORR) |
|-----------------|-------------------------------|

End point description:

ORR was defined as the percentage of subjects with measurable disease at baseline achieving a complete response (CR) or partial response (PR) according to modified response evaluation criteria in solid tumors (RECIST) criteria. RECIST criteria for CR: disappearance of all target lesions and non-target lesions, any pathological lymph nodes (whether target or non-target) must have reduction in short axis to <10 mm and normalization of tumor marker level. All lymph nodes must be non-pathological in size (<10 millimetre [mm] short axis). PR: At least a 30% decrease in the sum of the longest diameter (LD) of target lesions, taking as reference the baseline sum LD. Efficacy analysis set included ITT population- all randomized subjects regardless of whether they received any study treatment. Population included subjects with measurable disease at baseline.

|                      |           |
|----------------------|-----------|
| End point type       | Secondary |
| End point timeframe: |           |
| Up to 4.9 years      |           |

| End point values              | Abiraterone Acetate 1000 mg QD + Prednisone 5 mg BID | Abiraterone Acetate 1000 mg QD + Prednisone 5 mg QD | Abiraterone Acetate 1000 mg QD + Prednisone 2.5 mg BID | Abiraterone Acetate 1000 mg QD + Dexamethasone 0.5 mg QD |
|-------------------------------|--|---|--|--|
| Subject group type            | Reporting group                                      | Reporting group                                     | Reporting group  | Reporting group  |
| Number of subjects analysed   | 19   | 18  | 10   | 16   |
| Units: Percentage of subjects |  |   |  |  |
| number (not applicable)       | 42.1   | 38.9  | 60.0   | 56.3   |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Time to Opiate Use for Cancer-related Pain

End point title | Time to Opiate Use for Cancer-related Pain

End point description:

Time to opiate use for cancer-related pain is defined the time interval from the date of randomization to the first date of opiate use for cancer pain. Efficacy analysis set included ITT population- all randomized subjects regardless of whether they received any study treatment. '99999' indicates that median and 95% Confidence Interval (CI) were not estimable due to a limited number of events and the small sample size.

End point type | Secondary

End point timeframe:

Up to 156 weeks

| End point values                 | Abiraterone Acetate 1000 mg QD + Prednisone 5 mg BID | Abiraterone Acetate 1000 mg QD + Prednisone 5 mg QD | Abiraterone Acetate 1000 mg QD + Prednisone 2.5 mg BID | Abiraterone Acetate 1000 mg QD + Dexamethasone 0.5 mg QD |
|----------------------------------|--|---|--|--|
| Subject group type               | Reporting group                                      | Reporting group                                     | Reporting group  | Reporting group  |
| Number of subjects analysed      | 41   | 41  | 40   | 42   |
| Units: Months                    |  |   |  |  |
| median (confidence interval 95%) | 99999 (99999 to 99999)                               | 99999 (99999 to 99999)                              | 99999 (99999 to 99999)                                 | 99999 (99999 to 99999)                                   |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Time to Deterioration in Eastern Cooperative Oncology Group (ECOG) Performance Score by 1 Point

End point title | Time to Deterioration in Eastern Cooperative Oncology Group (ECOG) Performance Score by 1 Point

End point description:

Time to deterioration in ECOG Performance Status, the time interval from the date of randomization to the first date in which at least one point change (worsening) in the ECOG is observed during the main study treatment period. The ECOG performance status is a grade scale to measure quality of life (QoL). Scores run from 0 to 5, with 0 denoting perfect health and 5 denoting death. Efficacy analysis set included ITT population- all randomized subjects regardless of whether they received any study treatment. '99999' indicates that median and 95% Confidence Interval (CI) was not estimable due to a limited number of events and the small sample size.

End point type | Secondary

End point timeframe:

Up to 156 weeks

| <b>End point values</b>          | Abiraterone Acetate 1000 mg QD + Prednisone 5 mg BID | Abiraterone Acetate 1000 mg QD + Prednisone 5 mg QD | Abiraterone Acetate 1000 mg QD + Prednisone 2.5 mg BID | Abiraterone Acetate 1000 mg QD + Dexamethasone 0.5 mg QD |
|----------------------------------|--|---|--|--|
| Subject group type               | Reporting group                                      | Reporting group                                     | Reporting group  | Reporting group  |
| Number of subjects analysed      | 41   | 41  | 40   | 42   |
| Units: Months                    |  |   |  |  |
| median (confidence interval 95%) | 99999 (99999 to 99999)                               | 99999 (99999 to 99999)                              | 99999 (99999 to 99999)                                 | 99999 (23.95 to 99999)                                   |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Overall Survival

End point title Overall Survival

End point description:

Overall survival was defined as the time interval from the date of randomization to the date of death from any cause. Efficacy analysis set included ITT population- all randomized subjects regardless of whether they received any study treatment. Here '99999' indicates that median and upper limit of 95% Confidence Interval (CI) was not estimable due to a limited number of events and the small sample size.

End point type Secondary

End point timeframe:

Up to 4.9 years

| <b>End point values</b>          | Abiraterone Acetate 1000 mg QD + Prednisone 5 mg BID | Abiraterone Acetate 1000 mg QD + Prednisone 5 mg QD | Abiraterone Acetate 1000 mg QD + Prednisone 2.5 mg BID | Abiraterone Acetate 1000 mg QD + Dexamethasone 0.5 mg QD |
|----------------------------------|--|---|--|--|
| Subject group type               | Reporting group                                      | Reporting group                                     | Reporting group  | Reporting group  |
| Number of subjects analysed      | 41   | 41  | 40   | 42   |
| Units: Months                    |  |   |  |  |
| median (confidence interval 95%) | 34.07 (26.38 to 48.49)                               | 48.43 (39.95 to 99999)                              | 27.96 (23.66 to 40.51)                                 | 42.81 (30.23 to 99999)                                   |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Time to Next Prostate Cancer Therapy

|                        |  |
|------------------------|--|
| End point title        | Time to Next Prostate Cancer Therapy   |
| End point description: | Time to next prostate cancer therapy is defined as the time interval from the date of randomization to the date of initiation of first next therapy for prostate cancer. Efficacy analysis set included ITT population- all randomized subjects regardless of whether they received any study treatment. |
| End point type         | Secondary  |
| End point timeframe:   | Up to 4.9 years  |

| <b>End point values</b>          | Abiraterone Acetate 1000 mg QD + Prednisone 5 mg BID | Abiraterone Acetate 1000 mg QD + Prednisone 5 mg QD | Abiraterone Acetate 1000 mg QD + Prednisone 2.5 mg BID | Abiraterone Acetate 1000 mg QD + Dexamethasone 0.5 mg QD |
|----------------------------------|--|---|--|--|
| Subject group type               | Reporting group                                      | Reporting group                                     | Reporting group  | Reporting group  |
| Number of subjects analysed      | 41   | 41  | 40   | 42   |
| Units: Months                    |  |   |  |  |
| median (confidence interval 95%) | 20.14 (13.27 to 26.91)                               | 19.48 (12.09 to 33.08)                              | 16.66 (9.26 to 22.47)                                  | 28.29 (20.83 to 38.90)                                   |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Up to 4.9 years

Adverse event reporting additional description:

Safety population included all randomized and treated subjects.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 20.0 |
|--------------------|------|

### Reporting groups

|                       |  |
|-----------------------|--|
| Reporting group title | Abiraterone Acetate 1000 mg QD + Prednisone 5 mg BID |
|-----------------------|--|

Reporting group description:

Subjects received abiraterone acetate 1000 milligram (mg) tablet orally once daily (QD) and prednisone 5 mg tablet orally twice daily (BID) up to 156 Weeks. Subjects who were progression-free at 156 weeks entered the extension phase of the study and received study treatment until death, radiographic disease progression and/or unequivocal clinical progression, and/or other specific reasons for discontinuation. Subjects who ended the extension phase prematurely and subjects who did not enter the extension phase entered a follow-up phase until end of study.

|                       |   |
|-----------------------|---|
| Reporting group title | Abiraterone Acetate 1000 mg QD + Prednisone 5 mg QD |
|-----------------------|---|

Reporting group description:

Subjects received abiraterone acetate 1000 mg and prednisone 5 mg tablet orally QD up to 156 Weeks. Subjects who were progression-free at 156 weeks entered the extension phase of the study and received study treatment until death, radiographic disease progression and/or unequivocal clinical progression, and/or other specific reasons for discontinuation. Subjects who ended the extension phase prematurely and subjects who did not enter the extension phase entered a follow-up phase until end of study.

|                       |  |
|-----------------------|--|
| Reporting group title | Abiraterone Acetate 1000 mg QD + Prednisone 2.5 mg BID |
|-----------------------|--|

Reporting group description:

Subjects received abiraterone acetate 1000 mg tablet orally QD and prednisone 2.5 mg tablet orally BID up to 156 Weeks. Subjects who were progression free at 156 weeks entered the extension phase of the study and received study treatment until death, radiographic disease progression and/or unequivocal clinical progression, and/or other specific reasons for discontinuation. Subjects who ended the extension phase prematurely and subjects who did not enter the extension phase entered a follow-up phase until end of study.

|                       |  |
|-----------------------|--|
| Reporting group title | Abiraterone Acetate 1000 mg QD + Dexamethasone 0.5 mg QD |
|-----------------------|--|

Reporting group description:

Subjects received abiraterone acetate 1000 mg and dexamethasone 0.5 mg tablet orally QD up to 156 Weeks. Subjects who were progression free at 156 weeks entered the extension phase of the study and received study treatment until death, radiographic disease progression and/or unequivocal clinical progression, and/or other specific reasons for discontinuation. Subjects who ended the extension phase prematurely and subjects who did not enter the extension phase entered a follow-up phase until end of study.

| <b>Serious adverse events</b>                     | Abiraterone Acetate 1000 mg QD + Prednisone 5 mg BID | Abiraterone Acetate 1000 mg QD + Prednisone 5 mg QD | Abiraterone Acetate 1000 mg QD + Prednisone 2.5 mg BID |
|---|--|---|--|
| Total subjects affected by serious adverse events |  |   |  |
| subjects affected / exposed                       | 12 / 41 (29.27%)                                     | 10 / 41 (24.39%)                                    | 11 / 39 (28.21%)                                       |
| number of deaths (all causes)                     | 25   | 15  | 26   |
| number of deaths resulting from                   |  |   |  |

| adverse events  |                |                |                |
|---|----------------|----------------|----------------|
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                |                |                |
| Myelodysplastic Syndrome  |                |                |                |
| subjects affected / exposed   | 0 / 41 (0.00%) | 0 / 41 (0.00%) | 0 / 39 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          | 0 / 0          |
| Neuroendocrine Carcinoma of the Skin                                |                |                |                |
| subjects affected / exposed   | 0 / 41 (0.00%) | 0 / 41 (0.00%) | 0 / 39 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          | 0 / 0          |
| Vascular disorders  |                |                |                |
| Circulatory Collapse  |                |                |                |
| subjects affected / exposed   | 0 / 41 (0.00%) | 0 / 41 (0.00%) | 1 / 39 (2.56%) |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          | 0 / 0          |
| Deep Vein Thrombosis  |                |                |                |
| subjects affected / exposed   | 0 / 41 (0.00%) | 0 / 41 (0.00%) | 1 / 39 (2.56%) |
| occurrences causally related to treatment / all                     | 0 / 0          | 0 / 0          | 1 / 1          |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          | 0 / 0          |
| General disorders and administration site conditions                |                |                |                |
| Death   |                |                |                |
| subjects affected / exposed   | 0 / 41 (0.00%) | 1 / 41 (2.44%) | 0 / 39 (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          |
| General Physical Health Deterioration                               |                |                |                |
| subjects affected / exposed   | 1 / 41 (2.44%) | 0 / 41 (0.00%) | 0 / 39 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                          | 0 / 1          | 0 / 0          | 0 / 0          |
| Performance Status Decreased  |                |                |                |
| subjects affected / exposed   | 1 / 41 (2.44%) | 0 / 41 (0.00%) | 0 / 39 (0.00%) |
| occurrences causally related to treatment / all                     | 0 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all                          | 0 / 0          | 0 / 0          | 0 / 0          |
| Pyrexia   |                |                |                |

|  |                |                |                |
|--|----------------|----------------|----------------|
| subjects affected / exposed                            | 0 / 41 (0.00%) | 1 / 41 (2.44%) | 0 / 39 (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          |
| <b>Immune system disorders</b>                         |                |                |                |
| Hypersensitivity                                       |                |                |                |
| subjects affected / exposed                            | 1 / 41 (2.44%) | 0 / 41 (0.00%) | 0 / 39 (0.00%) |
| occurrences causally related to treatment / all        | 1 / 1          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all             | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Reproductive system and breast disorders</b>        |                |                |                |
| Pelvic Pain  |                |                |                |
| subjects affected / exposed                            | 1 / 41 (2.44%) | 0 / 41 (0.00%) | 0 / 39 (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          |
| <b>Respiratory, thoracic and mediastinal disorders</b> |                |                |                |
| Pleural Effusion                                       |                |                |                |
| subjects affected / exposed                            | 0 / 41 (0.00%) | 1 / 41 (2.44%) | 0 / 39 (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 Failure                                    |                |                |                |
| subjects affected / exposed                            | 0 / 41 (0.00%) | 0 / 41 (0.00%) | 1 / 39 (2.56%) |
| occurrences causally related to treatment / all        | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all             | 0 / 0          | 0 / 0          | 0 / 1          |
| <b>Psychiatric disorders</b>                           |                |                |                |
| Psychotic Disorder                                     |                |                |                |
| subjects affected / exposed                            | 0 / 41 (0.00%) | 0 / 41 (0.00%) | 0 / 39 (0.00%) |
| occurrences causally related to treatment / all        | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all             | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Product issues</b>                                  |                |                |                |
| Device Occlusion                                       |                |                |                |
| subjects affected / exposed                            | 1 / 41 (2.44%) | 0 / 41 (0.00%) | 0 / 39 (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          |
| <b>Injury, poisoning and procedural complications</b>  |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| Fall  |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 41 (0.00%) | 0 / 39 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Joint Injury                                    |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 1 / 41 (2.44%) | 0 / 39 (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          |
| Cardiac disorders                               |                |                |                |
| Atrial Flutter                                  |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 1 / 41 (2.44%) | 0 / 39 (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          |
| Atrioventricular Block Second Degree            |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 41 (0.00%) | 1 / 39 (2.56%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Bradycardia                                     |                |                |                |
| subjects affected / exposed                     | 1 / 41 (2.44%) | 0 / 41 (0.00%) | 0 / 39 (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 Failure                                 |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 41 (0.00%) | 1 / 39 (2.56%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Ventricular Arrhythmia                          |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 41 (0.00%) | 1 / 39 (2.56%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 1          |
| Nervous system disorders                        |                |                |                |
| Aphasia   |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 1 / 41 (2.44%) | 0 / 39 (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          |

|   |                |                |                |
|---|----------------|----------------|----------------|
| Cerebral Infarction                             |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 41 (0.00%) | 0 / 39 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Dementia Alzheimer's Type                       |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 1 / 41 (2.44%) | 0 / 39 (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          |
| Dizziness Postural                              |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 41 (0.00%) | 0 / 39 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Frontotemporal Dementia                         |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 41 (0.00%) | 0 / 39 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Haemorrhage Intracranial                        |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 41 (0.00%) | 1 / 39 (2.56%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Hypoaesthesia                                   |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 1 / 41 (2.44%) | 0 / 39 (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          |
| Hypokinesia                                     |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 41 (0.00%) | 1 / 39 (2.56%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Nerve Root Compression                          |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 41 (0.00%) | 1 / 39 (2.56%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Spinal Cord Compression                         |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 2 / 41 (4.88%) | 1 / 41 (2.44%) | 0 / 39 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2          | 0 / 1          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Syncope</b>                                  |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 1 / 41 (2.44%) | 1 / 39 (2.56%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Blood and lymphatic system disorders</b>     |                |                |                |
| <b>Anaemia of Malignant Disease</b>             |                |                |                |
| subjects affected / exposed                     | 1 / 41 (2.44%) | 0 / 41 (0.00%) | 0 / 39 (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          |
| <b>Neutropenia</b>                              |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 1 / 41 (2.44%) | 0 / 39 (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          |
| <b>Eye disorders</b>                            |                |                |                |
| <b>Vision Blurred</b>                           |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 41 (0.00%) | 1 / 39 (2.56%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| <b>Gastrointestinal disorders</b>               |                |                |                |
| <b>Abdominal Pain</b>                           |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 1 / 41 (2.44%) | 0 / 39 (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          |
| <b>Diarrhoea</b>                                |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 2 / 41 (4.88%) | 0 / 39 (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          |
| <b>Haematochezia</b>                            |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 41 (0.00%) | 0 / 39 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

|   |                |                |                |
|---|----------------|----------------|----------------|
| Incarcerated Inguinal Hernia<br>subjects affected / exposed | 0 / 41 (0.00%) | 0 / 41 (0.00%) | 1 / 39 (2.56%) |
| occurrences causally related to<br>treatment / all          | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to<br>treatment / all               | 0 / 0          | 0 / 0          | 0 / 0          |
| Inguinal Hernia<br>subjects affected / exposed              | 0 / 41 (0.00%) | 0 / 41 (0.00%) | 1 / 39 (2.56%) |
| occurrences causally related to<br>treatment / all          | 0 / 0          | 0 / 0          | 0 / 2          |
| deaths causally related to<br>treatment / all               | 0 / 0          | 0 / 0          | 0 / 0          |
| Melaena<br>subjects affected / exposed                      | 0 / 41 (0.00%) | 0 / 41 (0.00%) | 0 / 39 (0.00%) |
| occurrences causally related to<br>treatment / all          | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to<br>treatment / all               | 0 / 0          | 0 / 0          | 0 / 0          |
| Obstructive Pancreatitis<br>subjects affected / exposed     | 0 / 41 (0.00%) | 1 / 41 (2.44%) | 0 / 39 (0.00%) |
| occurrences causally related to<br>treatment / all          | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to<br>treatment / all               | 0 / 0          | 0 / 0          | 0 / 0          |
| Pancreatic Cyst<br>subjects affected / exposed              | 0 / 41 (0.00%) | 1 / 41 (2.44%) | 0 / 39 (0.00%) |
| occurrences causally related to<br>treatment / all          | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to<br>treatment / all               | 0 / 0          | 0 / 0          | 0 / 0          |
| Pancreatitis<br>subjects affected / exposed                 | 0 / 41 (0.00%) | 1 / 41 (2.44%) | 0 / 39 (0.00%) |
| occurrences causally related to<br>treatment / all          | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to<br>treatment / all               | 0 / 0          | 0 / 0          | 0 / 0          |
| Pancreatitis Acute<br>subjects affected / exposed           | 0 / 41 (0.00%) | 1 / 41 (2.44%) | 0 / 39 (0.00%) |
| occurrences causally related to<br>treatment / all          | 0 / 0          | 0 / 3          | 0 / 0          |
| deaths causally related to<br>treatment / all               | 0 / 0          | 0 / 0          | 0 / 0          |
| Vomiting<br>subjects affected / exposed                     | 0 / 41 (0.00%) | 1 / 41 (2.44%) | 0 / 39 (0.00%) |
| occurrences causally related to<br>treatment / all          | 0 / 0          | 0 / 1          | 0 / 0          |
| deaths causally related to<br>treatment / all               | 0 / 0          | 0 / 0          | 0 / 0          |
| Renal and urinary disorders                                 |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| Acute Kidney Injury                             |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 1 / 41 (2.44%) | 0 / 39 (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          |
| Bladder Tamponade                               |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 1 / 41 (2.44%) | 0 / 39 (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          |
| Haematuria                                      |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 41 (0.00%) | 1 / 39 (2.56%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Renal Colic                                     |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 41 (0.00%) | 1 / 39 (2.56%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Urinary Retention                               |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 41 (0.00%) | 1 / 39 (2.56%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Urinary Tract Obstruction                       |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 41 (0.00%) | 1 / 39 (2.56%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Musculoskeletal and connective tissue disorders |                |                |                |
| Arthropathy                                     |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 1 / 41 (2.44%) | 0 / 39 (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          |
| Back Pain                                       |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 2 / 41 (4.88%) | 1 / 39 (2.56%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 2          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

|   |                |                |                |
|---|----------------|----------------|----------------|
| Flank Pain                                      |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 41 (0.00%) | 0 / 39 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Intervertebral Disc Protrusion                  |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 41 (0.00%) | 1 / 39 (2.56%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Mobility Decreased                              |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 41 (0.00%) | 1 / 39 (2.56%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Osteoarthritis                                  |                |                |                |
| subjects affected / exposed                     | 2 / 41 (4.88%) | 0 / 41 (0.00%) | 0 / 39 (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          |
| Pathological Fracture                           |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 1 / 41 (2.44%) | 0 / 39 (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          |
| Infections and infestations                     |                |                |                |
| Diverticulitis                                  |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 41 (0.00%) | 0 / 39 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Lower Respiratory Tract Infection               |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 41 (0.00%) | 1 / 39 (2.56%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Pneumonia                                       |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 41 (0.00%) | 1 / 39 (2.56%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 1          |
| Sepsis  |                |                |                |

|   |                |                |                |
|---|----------------|----------------|----------------|
| subjects affected / exposed                     | 0 / 41 (0.00%) | 1 / 41 (2.44%) | 0 / 39 (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          |
| Urinary Tract Infection                         |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 41 (0.00%) | 1 / 39 (2.56%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 1          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |
| Metabolism and nutrition disorders              |                |                |                |
| Hypokalaemia                                    |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 1 / 41 (2.44%) | 0 / 39 (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          |
| Hyponatraemia                                   |                |                |                |
| subjects affected / exposed                     | 1 / 41 (2.44%) | 0 / 41 (0.00%) | 0 / 39 (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          |
| Ketosis   |                |                |                |
| subjects affected / exposed                     | 0 / 41 (0.00%) | 0 / 41 (0.00%) | 0 / 39 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          | 0 / 0          |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          | 0 / 0          |

|   |   |  |  |
|---|---|--|--|
| <b>Serious adverse events</b>                                       | Abiraterone Acetate<br>1000 mg QD +<br>Dexamethasone 0.5<br>mg QD |  |  |
| Total subjects affected by serious adverse events                   |   |  |  |
| subjects affected / exposed   | 18 / 42 (42.86%)  |  |  |
| number of deaths (all causes)                                       | 20  |  |  |
| number of deaths resulting from adverse events                      |   |  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |   |  |  |
| Myelodysplastic Syndrome  |   |  |  |
| subjects affected / exposed   | 1 / 42 (2.38%)  |  |  |
| occurrences causally related to treatment / all                     | 0 / 1   |  |  |
| deaths causally related to treatment / all                          | 0 / 0   |  |  |
| Neuroendocrine Carcinoma of the Skin                                |   |  |  |

|   |                |  |  |
|---|----------------|--|--|
| subjects affected / exposed                                 | 1 / 42 (2.38%) |  |  |
| occurrences causally related to treatment / all             | 0 / 1          |  |  |
| deaths causally related to treatment / all                  | 0 / 1          |  |  |
| <b>Vascular disorders</b>                                   |                |  |  |
| Circulatory Collapse  |                |  |  |
| subjects affected / exposed                                 | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all             | 0 / 0          |  |  |
| deaths causally related to treatment / all                  | 0 / 0          |  |  |
| Deep Vein Thrombosis  |                |  |  |
| subjects affected / exposed                                 | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all             | 0 / 0          |  |  |
| deaths causally related to treatment / all                  | 0 / 0          |  |  |
| <b>General disorders and administration site conditions</b> |                |  |  |
| Death   |                |  |  |
| subjects affected / exposed                                 | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all             | 0 / 0          |  |  |
| deaths causally related to treatment / all                  | 0 / 0          |  |  |
| General Physical Health Deterioration                       |                |  |  |
| subjects affected / exposed                                 | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all             | 0 / 0          |  |  |
| deaths causally related to treatment / all                  | 0 / 0          |  |  |
| Performance Status Decreased                                |                |  |  |
| subjects affected / exposed                                 | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all             | 0 / 0          |  |  |
| deaths causally related to treatment / all                  | 0 / 0          |  |  |
| Pyrexia   |                |  |  |
| subjects affected / exposed                                 | 2 / 42 (4.76%) |  |  |
| occurrences causally related to treatment / all             | 0 / 2          |  |  |
| deaths causally related to treatment / all                  | 0 / 0          |  |  |
| <b>Immune system disorders</b>                              |                |  |  |
| Hypersensitivity  |                |  |  |
| subjects affected / exposed                                 | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all             | 0 / 0          |  |  |
| deaths causally related to treatment / all                  | 0 / 0          |  |  |

|   |                                      |  |  |
|---|--------------------------------------|--|--|
| Reproductive system and breast disorders<br>Pelvic Pain<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all             | <br>0 / 42 (0.00%)<br>0 / 0<br>0 / 0 |  |  |
| Respiratory, thoracic and mediastinal disorders<br>Pleural Effusion<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all | <br>0 / 42 (0.00%)<br>0 / 0<br>0 / 0 |  |  |
| Respiratory Failure<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all   | <br>1 / 42 (2.38%)<br>0 / 1<br>0 / 1 |  |  |
| Psychiatric disorders<br>Psychotic Disorder<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                         | <br>1 / 42 (2.38%)<br>0 / 1<br>0 / 0 |  |  |
| Product issues<br>Device Occlusion<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all                                  | <br>0 / 42 (0.00%)<br>0 / 0<br>0 / 0 |  |  |
| Injury, poisoning and procedural complications<br>Fall<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all              | <br>1 / 42 (2.38%)<br>0 / 1<br>0 / 0 |  |  |
| Joint Injury<br>subjects affected / exposed<br>occurrences causally related to treatment / all<br>deaths causally related to treatment / all  | <br>0 / 42 (0.00%)<br>0 / 0<br>0 / 0 |  |  |
| Cardiac disorders   |                                      |  |  |

|   |                |  |  |
|---|----------------|--|--|
| Atrial Flutter                                  |                |  |  |
| subjects affected / exposed                     | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Atrioventricular Block Second Degree            |                |  |  |
| subjects affected / exposed                     | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Bradycardia                                     |                |  |  |
| subjects affected / exposed                     | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Cardiac Failure                                 |                |  |  |
| subjects affected / exposed                     | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Ventricular Arrhythmia                          |                |  |  |
| subjects affected / exposed                     | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Nervous system disorders                        |                |  |  |
| Aphasia   |                |  |  |
| subjects affected / exposed                     | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Cerebral Infarction                             |                |  |  |
| subjects affected / exposed                     | 1 / 42 (2.38%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Dementia Alzheimer's Type                       |                |  |  |
| subjects affected / exposed                     | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Dizziness Postural                              |                |  |  |

|   |                |  |  |
|---|----------------|--|--|
| subjects affected / exposed                     | 1 / 42 (2.38%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Frontotemporal Dementia</b>                  |                |  |  |
| subjects affected / exposed                     | 1 / 42 (2.38%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Haemorrhage Intracranial</b>                 |                |  |  |
| subjects affected / exposed                     | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Hypoaesthesia</b>                            |                |  |  |
| subjects affected / exposed                     | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Hypokinesia</b>                              |                |  |  |
| subjects affected / exposed                     | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Nerve Root Compression</b>                   |                |  |  |
| subjects affected / exposed                     | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Spinal Cord Compression</b>                  |                |  |  |
| subjects affected / exposed                     | 1 / 42 (2.38%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Syncope</b>                                  |                |  |  |
| subjects affected / exposed                     | 3 / 42 (7.14%) |  |  |
| occurrences causally related to treatment / all | 0 / 3          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Blood and lymphatic system disorders</b>     |                |  |  |
| Anaemia of Malignant Disease                    |                |  |  |

|   |                |  |  |
|---|----------------|--|--|
| subjects affected / exposed                     | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Neutropenia</b>                              |                |  |  |
| subjects affected / exposed                     | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Eye disorders</b>                            |                |  |  |
| Vision Blurred                                  |                |  |  |
| subjects affected / exposed                     | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Gastrointestinal disorders</b>               |                |  |  |
| Abdominal Pain                                  |                |  |  |
| subjects affected / exposed                     | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Diarrhoea                                       |                |  |  |
| subjects affected / exposed                     | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Haematochezia                                   |                |  |  |
| subjects affected / exposed                     | 1 / 42 (2.38%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Incarcerated Inguinal Hernia                    |                |  |  |
| subjects affected / exposed                     | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Inguinal Hernia                                 |                |  |  |
| subjects affected / exposed                     | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Melaena   |                |  |  |

|   |                |  |  |
|---|----------------|--|--|
| subjects affected / exposed                     | 1 / 42 (2.38%) |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Obstructive Pancreatitis</b>                 |                |  |  |
| subjects affected / exposed                     | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Pancreatic Cyst</b>                          |                |  |  |
| subjects affected / exposed                     | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Pancreatitis</b>                             |                |  |  |
| subjects affected / exposed                     | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Pancreatitis Acute</b>                       |                |  |  |
| subjects affected / exposed                     | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Vomiting</b>                                 |                |  |  |
| subjects affected / exposed                     | 1 / 42 (2.38%) |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Renal and urinary disorders</b>              |                |  |  |
| <b>Acute Kidney Injury</b>                      |                |  |  |
| subjects affected / exposed                     | 1 / 42 (2.38%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Bladder Tamponade</b>                        |                |  |  |
| subjects affected / exposed                     | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Haematuria</b>                               |                |  |  |

|  |                |  |  |
|--|----------------|--|--|
| subjects affected / exposed                            | 2 / 42 (4.76%) |  |  |
| occurrences causally related to treatment / all        | 0 / 2          |  |  |
| deaths causally related to treatment / all             | 0 / 0          |  |  |
| <b>Renal Colic</b>                                     |                |  |  |
| subjects affected / exposed                            | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all        | 0 / 0          |  |  |
| deaths causally related to treatment / all             | 0 / 0          |  |  |
| <b>Urinary Retention</b>                               |                |  |  |
| subjects affected / exposed                            | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all        | 0 / 0          |  |  |
| deaths causally related to treatment / all             | 0 / 0          |  |  |
| <b>Urinary Tract Obstruction</b>                       |                |  |  |
| subjects affected / exposed                            | 1 / 42 (2.38%) |  |  |
| occurrences causally related to treatment / all        | 0 / 1          |  |  |
| deaths causally related to treatment / all             | 0 / 0          |  |  |
| <b>Musculoskeletal and connective tissue disorders</b> |                |  |  |
| <b>Arthropathy</b>                                     |                |  |  |
| subjects affected / exposed                            | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all        | 0 / 0          |  |  |
| deaths causally related to treatment / all             | 0 / 0          |  |  |
| <b>Back Pain</b>                                       |                |  |  |
| subjects affected / exposed                            | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all        | 0 / 0          |  |  |
| deaths causally related to treatment / all             | 0 / 0          |  |  |
| <b>Flank Pain</b>                                      |                |  |  |
| subjects affected / exposed                            | 1 / 42 (2.38%) |  |  |
| occurrences causally related to treatment / all        | 0 / 1          |  |  |
| deaths causally related to treatment / all             | 0 / 0          |  |  |
| <b>Intervertebral Disc Protrusion</b>                  |                |  |  |
| subjects affected / exposed                            | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all        | 0 / 0          |  |  |
| deaths causally related to treatment / all             | 0 / 0          |  |  |
| <b>Mobility Decreased</b>                              |                |  |  |

|   |                |  |  |
|---|----------------|--|--|
| subjects affected / exposed                     | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Osteoarthritis</b>                           |                |  |  |
| subjects affected / exposed                     | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Pathological Fracture</b>                    |                |  |  |
| subjects affected / exposed                     | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Infections and infestations</b>              |                |  |  |
| <b>Diverticulitis</b>                           |                |  |  |
| subjects affected / exposed                     | 1 / 42 (2.38%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Lower Respiratory Tract Infection</b>        |                |  |  |
| subjects affected / exposed                     | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Pneumonia</b>                                |                |  |  |
| subjects affected / exposed                     | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Sepsis</b>                                   |                |  |  |
| subjects affected / exposed                     | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Urinary Tract Infection</b>                  |                |  |  |
| subjects affected / exposed                     | 1 / 42 (2.38%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| <b>Metabolism and nutrition disorders</b>       |                |  |  |

|   |                |  |  |
|---|----------------|--|--|
| Hypokalaemia                                    |                |  |  |
| subjects affected / exposed                     | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Hyponatraemia                                   |                |  |  |
| subjects affected / exposed                     | 0 / 42 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Ketosis   |                |  |  |
| subjects affected / exposed                     | 1 / 42 (2.38%) |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |

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

| <b>Non-serious adverse events</b>                                   | Abiraterone Acetate<br>1000 mg QD +<br>Prednisone 5 mg<br>BID | Abiraterone Acetate<br>1000 mg QD +<br>Prednisone 5 mg QD | Abiraterone Acetate<br>1000 mg QD +<br>Prednisone 2.5 mg<br>BID |
|---|---|---|---|
| Total subjects affected by non-serious adverse events               |   |   |   |
| subjects affected / exposed   | 39 / 41 (95.12%)  | 36 / 41 (87.80%)  | 37 / 39 (94.87%)  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |   |   |   |
| Basal Cell Carcinoma  |   |   |   |
| subjects affected / exposed   | 3 / 41 (7.32%)  | 0 / 41 (0.00%)  | 0 / 39 (0.00%)  |
| occurrences (all)   | 3   | 0   | 0   |
| Vascular disorders  |   |   |   |
| Hot Flush   |   |   |   |
| subjects affected / exposed   | 3 / 41 (7.32%)  | 1 / 41 (2.44%)  | 3 / 39 (7.69%)  |
| occurrences (all)   | 3   | 1   | 3   |
| Hypertension  |   |   |   |
| subjects affected / exposed   | 14 / 41 (34.15%)  | 22 / 41 (53.66%)  | 13 / 39 (33.33%)  |
| occurrences (all)   | 30  | 47  | 21  |
| General disorders and administration site conditions                |   |   |   |
| Asthenia  |   |   |   |
| subjects affected / exposed   | 3 / 41 (7.32%)  | 4 / 41 (9.76%)  | 1 / 39 (2.56%)  |
| occurrences (all)   | 6   | 8   | 1   |
| Chest Pain  |   |   |   |

|   |                       |                       |                      |
|---|-----------------------|-----------------------|----------------------|
| subjects affected / exposed<br>occurrences (all)  | 0 / 41 (0.00%)<br>0   | 3 / 41 (7.32%)<br>3   | 1 / 39 (2.56%)<br>2  |
| Fatigue<br>subjects affected / exposed<br>occurrences (all)   | 2 / 41 (4.88%)<br>2   | 6 / 41 (14.63%)<br>11 | 5 / 39 (12.82%)<br>5 |
| Influenza Like Illness<br>subjects affected / exposed<br>occurrences (all)                                      | 3 / 41 (7.32%)<br>5   | 0 / 41 (0.00%)<br>0   | 0 / 39 (0.00%)<br>0  |
| Oedema Peripheral<br>subjects affected / exposed<br>occurrences (all)   | 8 / 41 (19.51%)<br>10 | 4 / 41 (9.76%)<br>5   | 4 / 39 (10.26%)<br>5 |
| Pyrexia<br>subjects affected / exposed<br>occurrences (all)   | 1 / 41 (2.44%)<br>1   | 1 / 41 (2.44%)<br>1   | 2 / 39 (5.13%)<br>3  |
| Reproductive system and breast<br>disorders<br>Pelvic Pain<br>subjects affected / exposed<br>occurrences (all)  | 3 / 41 (7.32%)<br>7   | 2 / 41 (4.88%)<br>2   | 0 / 39 (0.00%)<br>0  |
| Respiratory, thoracic and mediastinal<br>disorders<br>Cough<br>subjects affected / exposed<br>occurrences (all) | 2 / 41 (4.88%)<br>2   | 1 / 41 (2.44%)<br>1   | 3 / 39 (7.69%)<br>3  |
| Investigations<br>Alanine Aminotransferase Increased<br>subjects affected / exposed<br>occurrences (all)        | 3 / 41 (7.32%)<br>12  | 2 / 41 (4.88%)<br>2   | 3 / 39 (7.69%)<br>3  |
| Aspartate Aminotransferase<br>Increased<br>subjects affected / exposed<br>occurrences (all)                     | 1 / 41 (2.44%)<br>6   | 2 / 41 (4.88%)<br>2   | 3 / 39 (7.69%)<br>4  |
| Blood Alkaline Phosphatase<br>Increased<br>subjects affected / exposed<br>occurrences (all)                     | 1 / 41 (2.44%)<br>1   | 1 / 41 (2.44%)<br>1   | 1 / 39 (2.56%)<br>1  |
| Blood Bilirubin Increased   |                       |                       |                      |

|  |                       |                      |                        |
|--|-----------------------|----------------------|------------------------|
| subjects affected / exposed<br>occurrences (all)   | 3 / 41 (7.32%)<br>3   | 0 / 41 (0.00%)<br>0  | 1 / 39 (2.56%)<br>2    |
| Blood Lactate Dehydrogenase Increased<br>subjects affected / exposed<br>occurrences (all)                  | 0 / 41 (0.00%)<br>0   | 0 / 41 (0.00%)<br>0  | 2 / 39 (5.13%)<br>2    |
| C-Reactive Protein Increased<br>subjects affected / exposed<br>occurrences (all)                           | 0 / 41 (0.00%)<br>0   | 0 / 41 (0.00%)<br>0  | 2 / 39 (5.13%)<br>2    |
| Hepatic Enzyme Increased<br>subjects affected / exposed<br>occurrences (all)                               | 0 / 41 (0.00%)<br>0   | 0 / 41 (0.00%)<br>0  | 0 / 39 (0.00%)<br>0    |
| Weight Decreased<br>subjects affected / exposed<br>occurrences (all)                                       | 7 / 41 (17.07%)<br>11 | 7 / 41 (17.07%)<br>9 | 10 / 39 (25.64%)<br>12 |
| Weight Increased<br>subjects affected / exposed<br>occurrences (all)                                       | 4 / 41 (9.76%)<br>6   | 2 / 41 (4.88%)<br>4  | 1 / 39 (2.56%)<br>1    |
| Injury, poisoning and procedural complications<br>Fall<br>subjects affected / exposed<br>occurrences (all) | 3 / 41 (7.32%)<br>3   | 0 / 41 (0.00%)<br>0  | 0 / 39 (0.00%)<br>0    |
| Nervous system disorders<br>Headache<br>subjects affected / exposed<br>occurrences (all)                   | 2 / 41 (4.88%)<br>2   | 2 / 41 (4.88%)<br>2  | 2 / 39 (5.13%)<br>3    |
| Paraesthesia<br>subjects affected / exposed<br>occurrences (all)   | 0 / 41 (0.00%)<br>0   | 0 / 41 (0.00%)<br>0  | 2 / 39 (5.13%)<br>2    |
| Blood and lymphatic system disorders<br>Anaemia<br>subjects affected / exposed<br>occurrences (all)        | 1 / 41 (2.44%)<br>1   | 1 / 41 (2.44%)<br>1  | 1 / 39 (2.56%)<br>1    |
| Gastrointestinal disorders<br>Abdominal Pain<br>subjects affected / exposed<br>occurrences (all)           | 4 / 41 (9.76%)<br>5   | 2 / 41 (4.88%)<br>3  | 1 / 39 (2.56%)<br>1    |

|  |                       |                       |                     |
|--|-----------------------|-----------------------|---------------------|
| Abdominal Pain Upper<br>subjects affected / exposed<br>occurrences (all) | 2 / 41 (4.88%)<br>2   | 1 / 41 (2.44%)<br>1   | 3 / 39 (7.69%)<br>3 |
| Constipation<br>subjects affected / exposed<br>occurrences (all)         | 9 / 41 (21.95%)<br>9  | 4 / 41 (9.76%)<br>5   | 3 / 39 (7.69%)<br>4 |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)            | 3 / 41 (7.32%)<br>3   | 3 / 41 (7.32%)<br>8   | 2 / 39 (5.13%)<br>2 |
| Dry Mouth<br>subjects affected / exposed<br>occurrences (all)            | 1 / 41 (2.44%)<br>1   | 0 / 41 (0.00%)<br>0   | 2 / 39 (5.13%)<br>2 |
| Nausea<br>subjects affected / exposed<br>occurrences (all)               | 1 / 41 (2.44%)<br>1   | 2 / 41 (4.88%)<br>3   | 2 / 39 (5.13%)<br>2 |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)             | 2 / 41 (4.88%)<br>2   | 2 / 41 (4.88%)<br>2   | 2 / 39 (5.13%)<br>2 |
| Skin and subcutaneous tissue disorders                                   |                       |                       |                     |
| Hyperhidrosis<br>subjects affected / exposed<br>occurrences (all)        | 2 / 41 (4.88%)<br>2   | 0 / 41 (0.00%)<br>0   | 3 / 39 (7.69%)<br>3 |
| Skin Atrophy<br>subjects affected / exposed<br>occurrences (all)         | 0 / 41 (0.00%)<br>0   | 0 / 41 (0.00%)<br>0   | 0 / 39 (0.00%)<br>0 |
| Renal and urinary disorders  |                       |                       |                     |
| Haematuria<br>subjects affected / exposed<br>occurrences (all)           | 2 / 41 (4.88%)<br>3   | 1 / 41 (2.44%)<br>1   | 2 / 39 (5.13%)<br>3 |
| Urinary Retention<br>subjects affected / exposed<br>occurrences (all)    | 2 / 41 (4.88%)<br>2   | 3 / 41 (7.32%)<br>3   | 0 / 39 (0.00%)<br>0 |
| Musculoskeletal and connective tissue disorders                          |                       |                       |                     |
| Arthralgia<br>subjects affected / exposed<br>occurrences (all)           | 9 / 41 (21.95%)<br>14 | 9 / 41 (21.95%)<br>12 | 2 / 39 (5.13%)<br>2 |

|                             |                  |                 |                  |
|-----------------------------|------------------|-----------------|------------------|
| Back Pain                   |                  |                 |                  |
| subjects affected / exposed | 13 / 41 (31.71%) | 5 / 41 (12.20%) | 10 / 39 (25.64%) |
| occurrences (all)           | 16               | 8               | 13               |
| Bone Pain                   |                  |                 |                  |
| subjects affected / exposed | 11 / 41 (26.83%) | 3 / 41 (7.32%)  | 5 / 39 (12.82%)  |
| occurrences (all)           | 14               | 4               | 7                |
| Groin Pain                  |                  |                 |                  |
| subjects affected / exposed | 1 / 41 (2.44%)   | 0 / 41 (0.00%)  | 2 / 39 (5.13%)   |
| occurrences (all)           | 1                | 0               | 3                |
| Muscle Spasms               |                  |                 |                  |
| subjects affected / exposed | 4 / 41 (9.76%)   | 1 / 41 (2.44%)  | 4 / 39 (10.26%)  |
| occurrences (all)           | 7                | 1               | 4                |
| Musculoskeletal Pain        |                  |                 |                  |
| subjects affected / exposed | 3 / 41 (7.32%)   | 1 / 41 (2.44%)  | 2 / 39 (5.13%)   |
| occurrences (all)           | 3                | 1               | 3                |
| Myalgia                     |                  |                 |                  |
| subjects affected / exposed | 2 / 41 (4.88%)   | 5 / 41 (12.20%) | 0 / 39 (0.00%)   |
| occurrences (all)           | 2                | 5               | 0                |
| Osteopenia                  |                  |                 |                  |
| subjects affected / exposed | 3 / 41 (7.32%)   | 3 / 41 (7.32%)  | 0 / 39 (0.00%)   |
| occurrences (all)           | 3                | 3               | 0                |
| Osteoporosis                |                  |                 |                  |
| subjects affected / exposed | 1 / 41 (2.44%)   | 1 / 41 (2.44%)  | 1 / 39 (2.56%)   |
| occurrences (all)           | 1                | 1               | 1                |
| Pain in Extremity           |                  |                 |                  |
| subjects affected / exposed | 5 / 41 (12.20%)  | 2 / 41 (4.88%)  | 4 / 39 (10.26%)  |
| occurrences (all)           | 6                | 2               | 7                |
| Infections and infestations |                  |                 |                  |
| Bronchitis                  |                  |                 |                  |
| subjects affected / exposed | 0 / 41 (0.00%)   | 2 / 41 (4.88%)  | 0 / 39 (0.00%)   |
| occurrences (all)           | 0                | 2               | 0                |
| Nasopharyngitis             |                  |                 |                  |
| subjects affected / exposed | 3 / 41 (7.32%)   | 1 / 41 (2.44%)  | 3 / 39 (7.69%)   |
| occurrences (all)           | 3                | 1               | 5                |
| Urinary Tract Infection     |                  |                 |                  |

|  |                      |                       |                      |
|--|----------------------|-----------------------|----------------------|
| subjects affected / exposed<br>occurrences (all)   | 1 / 41 (2.44%)<br>1  | 4 / 41 (9.76%)<br>5   | 0 / 39 (0.00%)<br>0  |
| Metabolism and nutrition disorders<br>Decreased Appetite<br>subjects affected / exposed<br>occurrences (all) | 1 / 41 (2.44%)<br>2  | 1 / 41 (2.44%)<br>1   | 2 / 39 (5.13%)<br>2  |
| Hypokalaemia<br>subjects affected / exposed<br>occurrences (all)   | 5 / 41 (12.20%)<br>6 | 7 / 41 (17.07%)<br>13 | 7 / 39 (17.95%)<br>9 |

|  |   |  |  |
|--|---|--|--|
| <b>Non-serious adverse events</b>  | Abiraterone Acetate<br>1000 mg QD +<br>Dexamethasone 0.5<br>mg QD |  |  |
| Total subjects affected by non-serious<br>adverse events<br>subjects affected / exposed  | 39 / 42 (92.86%)  |  |  |
| Neoplasms benign, malignant and<br>unspecified (incl cysts and polyps)<br>Basal Cell Carcinoma<br>subjects affected / exposed<br>occurrences (all) | 0 / 42 (0.00%)<br>0   |  |  |
| Vascular disorders<br>Hot Flush<br>subjects affected / exposed<br>occurrences (all)  | 5 / 42 (11.90%)<br>6  |  |  |
| Hypertension<br>subjects affected / exposed<br>occurrences (all)   | 10 / 42 (23.81%)<br>16  |  |  |
| General disorders and administration<br>site conditions<br>Asthenia<br>subjects affected / exposed<br>occurrences (all)                            | 1 / 42 (2.38%)<br>1   |  |  |
| Chest Pain<br>subjects affected / exposed<br>occurrences (all)   | 1 / 42 (2.38%)<br>1   |  |  |
| Fatigue<br>subjects affected / exposed<br>occurrences (all)  | 7 / 42 (16.67%)<br>7  |  |  |
| Influenza Like Illness   |   |  |  |

|  |                       |  |  |
|--|-----------------------|--|--|
| subjects affected / exposed<br>occurrences (all)   | 0 / 42 (0.00%)<br>0   |  |  |
| Oedema Peripheral<br>subjects affected / exposed<br>occurrences (all)  | 8 / 42 (19.05%)<br>12 |  |  |
| Pyrexia<br>subjects affected / exposed<br>occurrences (all)  | 1 / 42 (2.38%)<br>1   |  |  |
| Reproductive system and breast disorders<br>Pelvic Pain<br>subjects affected / exposed<br>occurrences (all)  | 2 / 42 (4.76%)<br>2   |  |  |
| Respiratory, thoracic and mediastinal disorders<br>Cough<br>subjects affected / exposed<br>occurrences (all) | 0 / 42 (0.00%)<br>0   |  |  |
| Investigations<br>Alanine Aminotransferase Increased<br>subjects affected / exposed<br>occurrences (all)     | 5 / 42 (11.90%)<br>10 |  |  |
| Aspartate Aminotransferase Increased<br>subjects affected / exposed<br>occurrences (all)                     | 4 / 42 (9.52%)<br>7   |  |  |
| Blood Alkaline Phosphatase Increased<br>subjects affected / exposed<br>occurrences (all)                     | 3 / 42 (7.14%)<br>4   |  |  |
| Blood Bilirubin Increased<br>subjects affected / exposed<br>occurrences (all)                                | 0 / 42 (0.00%)<br>0   |  |  |
| Blood Lactate Dehydrogenase Increased<br>subjects affected / exposed<br>occurrences (all)                    | 0 / 42 (0.00%)<br>0   |  |  |
| C-Reactive Protein Increased   |                       |  |  |

|  |                      |  |  |
|--|----------------------|--|--|
| subjects affected / exposed<br>occurrences (all)   | 0 / 42 (0.00%)<br>0  |  |  |
| Hepatic Enzyme Increased<br>subjects affected / exposed<br>occurrences (all)                               | 3 / 42 (7.14%)<br>13 |  |  |
| Weight Decreased<br>subjects affected / exposed<br>occurrences (all)                                       | 3 / 42 (7.14%)<br>3  |  |  |
| Weight Increased<br>subjects affected / exposed<br>occurrences (all)                                       | 6 / 42 (14.29%)<br>8 |  |  |
| Injury, poisoning and procedural complications<br>Fall<br>subjects affected / exposed<br>occurrences (all) | 2 / 42 (4.76%)<br>4  |  |  |
| Nervous system disorders<br>Headache<br>subjects affected / exposed<br>occurrences (all)                   | 3 / 42 (7.14%)<br>3  |  |  |
| Paraesthesia<br>subjects affected / exposed<br>occurrences (all)   | 2 / 42 (4.76%)<br>2  |  |  |
| Blood and lymphatic system disorders<br>Anaemia<br>subjects affected / exposed<br>occurrences (all)        | 4 / 42 (9.52%)<br>5  |  |  |
| Gastrointestinal disorders<br>Abdominal Pain<br>subjects affected / exposed<br>occurrences (all)           | 0 / 42 (0.00%)<br>0  |  |  |
| Abdominal Pain Upper<br>subjects affected / exposed<br>occurrences (all)                                   | 2 / 42 (4.76%)<br>2  |  |  |
| Constipation<br>subjects affected / exposed<br>occurrences (all)   | 2 / 42 (4.76%)<br>2  |  |  |

|   |                       |  |  |
|---|-----------------------|--|--|
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)   | 1 / 42 (2.38%)<br>2   |  |  |
| Dry Mouth<br>subjects affected / exposed<br>occurrences (all)   | 0 / 42 (0.00%)<br>0   |  |  |
| Nausea<br>subjects affected / exposed<br>occurrences (all)  | 3 / 42 (7.14%)<br>3   |  |  |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)  | 2 / 42 (4.76%)<br>2   |  |  |
| Skin and subcutaneous tissue disorders<br>Hyperhidrosis<br>subjects affected / exposed<br>occurrences (all)       | 1 / 42 (2.38%)<br>2   |  |  |
| Skin Atrophy<br>subjects affected / exposed<br>occurrences (all)  | 3 / 42 (7.14%)<br>3   |  |  |
| Renal and urinary disorders<br>Haematuria<br>subjects affected / exposed<br>occurrences (all)                     | 3 / 42 (7.14%)<br>3   |  |  |
| Urinary Retention<br>subjects affected / exposed<br>occurrences (all)   | 1 / 42 (2.38%)<br>1   |  |  |
| Musculoskeletal and connective tissue disorders<br>Arthralgia<br>subjects affected / exposed<br>occurrences (all) | 2 / 42 (4.76%)<br>2   |  |  |
| Back Pain<br>subjects affected / exposed<br>occurrences (all)   | 9 / 42 (21.43%)<br>13 |  |  |
| Bone Pain<br>subjects affected / exposed<br>occurrences (all)   | 2 / 42 (4.76%)<br>2   |  |  |

|                                    |                |  |  |
|------------------------------------|----------------|--|--|
| Groin Pain                         |                |  |  |
| subjects affected / exposed        | 0 / 42 (0.00%) |  |  |
| occurrences (all)                  | 0              |  |  |
| Muscle Spasms                      |                |  |  |
| subjects affected / exposed        | 2 / 42 (4.76%) |  |  |
| occurrences (all)                  | 3              |  |  |
| Musculoskeletal Pain               |                |  |  |
| subjects affected / exposed        | 2 / 42 (4.76%) |  |  |
| occurrences (all)                  | 3              |  |  |
| Myalgia                            |                |  |  |
| subjects affected / exposed        | 0 / 42 (0.00%) |  |  |
| occurrences (all)                  | 0              |  |  |
| Osteopenia                         |                |  |  |
| subjects affected / exposed        | 1 / 42 (2.38%) |  |  |
| occurrences (all)                  | 1              |  |  |
| Osteoporosis                       |                |  |  |
| subjects affected / exposed        | 3 / 42 (7.14%) |  |  |
| occurrences (all)                  | 3              |  |  |
| Pain in Extremity                  |                |  |  |
| subjects affected / exposed        | 3 / 42 (7.14%) |  |  |
| occurrences (all)                  | 4              |  |  |
| Infections and infestations        |                |  |  |
| Bronchitis                         |                |  |  |
| subjects affected / exposed        | 3 / 42 (7.14%) |  |  |
| occurrences (all)                  | 4              |  |  |
| Nasopharyngitis                    |                |  |  |
| subjects affected / exposed        | 2 / 42 (4.76%) |  |  |
| occurrences (all)                  | 2              |  |  |
| Urinary Tract Infection            |                |  |  |
| subjects affected / exposed        | 3 / 42 (7.14%) |  |  |
| occurrences (all)                  | 3              |  |  |
| Metabolism and nutrition disorders |                |  |  |
| Decreased Appetite                 |                |  |  |
| subjects affected / exposed        | 1 / 42 (2.38%) |  |  |
| occurrences (all)                  | 1              |  |  |
| Hypokalaemia                       |                |  |  |

|                             |                 |  |  |
|-----------------------------|-----------------|--|--|
| subjects affected / exposed | 7 / 42 (16.67%) |  |  |
| occurrences (all)           | 11              |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment  |
|------------------|--|
| 13 November 2013 | Amendment INT-2 included following changes: Adjusted inclusion/exclusion criteria to include subjects with liver or lung visceral metastases, subjects treated with a maximum of 2 anti-hypertensives, and subjects who previously received palliative radiotherapy for prostate cancer; adjusted exclusion criteria to exclude subjects who received prior corticosteroid treatment for prostate cancer; modified birth control requirements during the study; clarified procedural aspects of the study, including definitions of study completion and procedures associated with discontinuation; clarified concomitant therapy during the main study treatment period and extension phase. |
| 27 November 2014 | Amendment INT-4 included following changes: Referenced additional information on potential drug-drug interactions, including those related to CYP1A2, CYP2D6, and CYP2C8; clarified the scope and timing of data analyses; described dosing compliance procedures.   |

Notes:

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### 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.

Study not designed/powerd to allow comparisons in study groups. Per protocol amendment 6, the study was ended earlier since sufficient extension and follow-up data have been collected to allow statistical analysis of secondary objectives.

Notes: