



## Clinical trial results: A Phase 3b Multicenter, Open-label Abiraterone Acetate Long-term Safety Study Summary

|                          |                      |
|--------------------------|----------------------|
| EudraCT number           | 2011-005243-28       |
| Trial protocol           | BE HU ES AT GB DE SE |
| Global end of trial date | 22 April 2021        |

### Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1 (current) |
| This version publication date  | 05 May 2022  |
| First version publication date | 05 May 2022  |

### Trial information

#### Trial identification

|                       |               |
|-----------------------|---------------|
| Sponsor protocol code | 212082PCR3010 |
|-----------------------|---------------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01517802 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

|                              |                                                                                               |
|------------------------------|-----------------------------------------------------------------------------------------------|
| Sponsor organisation name    | Janssen Research & Development, LLC                                                           |
| Sponsor organisation address | 920 Route 202, Raritan, United States, 08869                                                  |
| Public contact               | Clinical Registry group, Janssen Research & Development, LLC,<br>ClinicalTrialsEU@its.jnj.com |
| Scientific contact           | Clinical Registry group, Janssen Research & Development, LLC,<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                       | 22 April 2021 |
| Is this the analysis of the primary completion data? | No            |
| Global end of trial reached?                         | Yes           |
| Global end of trial date                             | 22 April 2021 |
| Was the trial ended prematurely?                     | No            |

Notes:

## General information about the trial

Main objective of the trial:

The main objective of the trial was to provide abiraterone acetate and collect long-term follow-up safety data from subjects who completed abiraterone acetate studies for a maximum duration of 9 years from the study protocol INT-1 issue date (9 April 2012).

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 Practice (GCP) and applicable regulatory requirements. Safety assessment included monitoring of serious adverse events.

Background therapy: -

Evidence for comparator: -

|                                                           |                  |
|-----------------------------------------------------------|------------------|
| Actual start date of recruitment                          | 12 February 2013 |
| Long term follow-up planned                               | Yes              |
| Long term follow-up rationale                             | Safety           |
| Long term follow-up duration                              | 9 Years          |
| Independent data monitoring committee (IDMC) involvement? | No               |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                   |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Australia: 4      |
| Country: Number of subjects enrolled | Belgium: 2        |
| Country: Number of subjects enrolled | Germany: 1        |
| Country: Number of subjects enrolled | Spain: 1          |
| Country: Number of subjects enrolled | United Kingdom: 6 |
| Country: Number of subjects enrolled | United States: 16 |
| Country: Number of subjects enrolled | Sweden: 1         |
| Worldwide total number of subjects   | 31                |
| EEA total number of subjects         | 5                 |

Notes:

### Subjects enrolled per age group

|                                           |   |
|-------------------------------------------|---|
| In utero                                  | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days)                      | 0 |

|                                          |    |
|------------------------------------------|----|
| Infants and toddlers (28 days-23 months) | 0  |
| Children (2-11 years)                    | 0  |
| Adolescents (12-17 years)                | 0  |
| Adults (18-64 years)                     | 2  |
| From 65 to 84 years                      | 12 |
| 85 years and over                        | 17 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Out of 32 enrolled subjects, 1 subject did not receive any dose of drug and hence was excluded from all the analyses.

### Period 1

|                              |                          |
|------------------------------|--------------------------|
| Period 1 title               | Overall (overall period) |
| Is this the baseline period? | Yes                      |
| Allocation method            | Not applicable           |
| Blinding used                | Not blinded              |

### Arms

|                  |                                               |
|------------------|-----------------------------------------------|
| <b>Arm title</b> | Abiraterone Acetate + Prednisone/Prednisolone |
|------------------|-----------------------------------------------|

Arm description:

Subjects who received at least 3 months of abiraterone acetate treatment in previously completed abiraterone acetate studies (COU-AA-001 [NCT00473512], COU-AA-002 [NCT00473746], COU-AA-006 [NCT00910754], COU-AA-206 [NCT01400555], COU-AA-301 [NCT00638690], COU-AA-302 [NCT00887198], COU-AA-BMA [NCT00544440]) continued to receive abiraterone acetate 1000 milligrams (mg) (four 250 mg tablets) along with low dose corticosteroid (prednisone/prednisolone) 5 mg tablet orally twice daily starting Day 1 Cycle 1 (each cycle was of 28 days) according to dosing regimen established in the previously completed study until the investigator determined that the subject no longer received benefit or the sponsor terminated the study or the subject had continued the treatment in this study and were followed-up for safety for up to 9 years.

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

Dosage and administration details:

Prednisone/Prednisolone 5 mg tablet was administered orally twice daily.

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

Dosage and administration details:

Abiraterone Acetate 1000 mg (four 250 mg tablets) was administered orally once daily.

|                                       |                                               |
|---------------------------------------|-----------------------------------------------|
| <b>Number of subjects in period 1</b> | Abiraterone Acetate + Prednisone/Prednisolone |
| Started                               | 31                                            |
| Completed                             | 30                                            |
| Not completed                         | 1                                             |
| Adverse event, serious fatal          | 1                                             |



## Baseline characteristics

### Reporting groups

|                       |                                               |
|-----------------------|-----------------------------------------------|
| Reporting group title | Abiraterone Acetate + Prednisone/Prednisolone |
|-----------------------|-----------------------------------------------|

Reporting group description:

Subjects who received at least 3 months of abiraterone acetate treatment in previously completed abiraterone acetate studies (COU-AA-001 [NCT00473512], COU-AA-002 [NCT00473746], COU-AA-006 [NCT00910754], COU-AA-206 [NCT01400555], COU-AA-301 [NCT00638690], COU-AA-302 [NCT00887198], COU-AA-BMA [NCT00544440]) continued to receive abiraterone acetate 1000 milligrams (mg) (four 250 mg tablets) along with low dose corticosteroid (prednisone/prednisolone) 5 mg tablet orally twice daily starting Day 1 Cycle 1 (each cycle was of 28 days) according to dosing regimen established in the previously completed study until the investigator determined that the subject no longer received benefit or the sponsor terminated the study or the subject had continued the treatment in this study and were followed-up for safety for up to 9 years.

| Reporting group values                             | Abiraterone Acetate + Prednisone/Prednisolone | Total |  |
|----------------------------------------------------|-----------------------------------------------|-------|--|
| Number of subjects                                 | 31                                            | 31    |  |
| Age Categorical<br>Units: Subjects                 |                                               |       |  |
| In utero                                           | 0                                             | 0     |  |
| Preterm newborn infants (gestational age < 37 wks) | 0                                             | 0     |  |
| Newborns (0-27 days)                               | 0                                             | 0     |  |
| Infants and toddlers (28 days-23 months)           | 0                                             | 0     |  |
| Children (2-11 years)                              | 0                                             | 0     |  |
| Adolescents (12-17 years)                          | 0                                             | 0     |  |
| Adults (18-64 years)                               | 2                                             | 2     |  |
| From 65-84 years                                   | 12                                            | 12    |  |
| 85 years and over                                  | 17                                            | 17    |  |
| Gender Categorical<br>Units: Subjects              |                                               |       |  |
| Female                                             | 0                                             | 0     |  |
| Male                                               | 31                                            | 31    |  |

## End points

### End points reporting groups

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                               |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------|
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | Abiraterone Acetate + Prednisone/Prednisolone |
| Reporting group description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                               |
| Subjects who received at least 3 months of abiraterone acetate treatment in previously completed abiraterone acetate studies (COU-AA-001 [NCT00473512], COU-AA-002 [NCT00473746], COU-AA-006 [NCT00910754], COU-AA-206 [NCT01400555], COU-AA-301 [NCT00638690], COU-AA-302 [NCT00887198], COU-AA-BMA [NCT00544440]) continued to receive abiraterone acetate 1000 milligrams (mg) (four 250 mg tablets) along with low dose corticosteroid (prednisone/prednisolone) 5 mg tablet orally twice daily starting Day 1 Cycle 1 (each cycle was of 28 days) according to dosing regimen established in the previously completed study until the investigator determined that the subject no longer received benefit or the sponsor terminated the study or the subject had continued the treatment in this study and were followed-up for safety for up to 9 years. |                                               |

### Primary: Number of Subjects with Serious Adverse Events (SAEs)

|                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                      |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                             | Number of Subjects with Serious Adverse Events (SAEs) <sup>[1]</sup> |
| End point description:                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                      |
| An SAE is defined as any untoward medical occurrence that results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, leads to a congenital anomaly/birth defect in the offspring of a subject, or is an important medical event. Safety analysis set included subjects that received at least 1 dose of study drug. |                                                                      |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                              | Primary                                                              |
| End point timeframe:                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                      |
| Up to 9 years                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                      |

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: No Inferential statistical analysis was planned for the Primary Endpoint.

|                             |                                               |  |  |  |
|-----------------------------|-----------------------------------------------|--|--|--|
| <b>End point values</b>     | Abiraterone Acetate + Prednisone/Prednisolone |  |  |  |
| Subject group type          | Reporting group                               |  |  |  |
| Number of subjects analysed | 31                                            |  |  |  |
| Units: subjects             | 16                                            |  |  |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information<sup>[1]</sup>

Timeframe for reporting adverse events:

up to 9 years

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 23.0 |
|--------------------|------|

### Reporting groups

|                       |                                               |
|-----------------------|-----------------------------------------------|
| Reporting group title | Abiraterone Acetate + Prednisone/Prednisolone |
|-----------------------|-----------------------------------------------|

Reporting group description:

Subjects who received at least 3 months of abiraterone acetate treatment in previously completed abiraterone acetate studies (COU-AA-001 [NCT00473512], COU-AA-002 [NCT00473746], COU-AA-006 [NCT00910754], COU-AA-206 [NCT01400555], COU-AA-301 [NCT00638690], COU-AA-302 [NCT00887198], COU-AA-BMA [NCT00544440]) continued to receive abiraterone acetate 1000 milligrams (mg) (four 250 mg tablets) tablet along with low dose corticosteroid (prednisone/prednisolone) 5 mg tablet orally twice daily starting Day 1 Cycle 1 (each cycle was of 28 days) according to dosing regimen established in the previously completed study until the investigator determined that the subject no longer received benefit or the sponsor terminated the study or the subject had continued the treatment in this study and were followed-up for safety for up to 9 years.

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: No other adverse events were collected and analyzed.

| Serious adverse events                            | Abiraterone Acetate + Prednisone/Prednisolone |  |  |
|---------------------------------------------------|-----------------------------------------------|--|--|
| Total subjects affected by serious adverse events |                                               |  |  |
| subjects affected / exposed                       | 16 / 31 (51.61%)                              |  |  |
| number of deaths (all causes)                     | 1                                             |  |  |
| number of deaths resulting from adverse events    |                                               |  |  |
| Vascular disorders                                |                                               |  |  |
| Aortic thrombosis                                 |                                               |  |  |
| subjects affected / exposed                       | 1 / 31 (3.23%)                                |  |  |
| occurrences causally related to treatment / all   | 0 / 1                                         |  |  |
| deaths causally related to treatment / all        | 0 / 0                                         |  |  |
| Hypertension                                      |                                               |  |  |
| subjects affected / exposed                       | 1 / 31 (3.23%)                                |  |  |
| occurrences causally related to treatment / all   | 0 / 1                                         |  |  |
| deaths causally related to treatment / all        | 0 / 0                                         |  |  |
| Surgical and medical procedures                   |                                               |  |  |
| Aortic valve replacement                          |                                               |  |  |



|                                                      |                |  |  |
|------------------------------------------------------|----------------|--|--|
| subjects affected / exposed                          | 1 / 31 (3.23%) |  |  |
| occurrences causally related to treatment / all      | 0 / 1          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| General disorders and administration site conditions |                |  |  |
| Fatigue                                              |                |  |  |
| subjects affected / exposed                          | 1 / 31 (3.23%) |  |  |
| occurrences causally related to treatment / all      | 0 / 1          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Respiratory, thoracic and mediastinal disorders      |                |  |  |
| Dyspnoea                                             |                |  |  |
| subjects affected / exposed                          | 1 / 31 (3.23%) |  |  |
| occurrences causally related to treatment / all      | 0 / 1          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Pulmonary embolism                                   |                |  |  |
| subjects affected / exposed                          | 3 / 31 (9.68%) |  |  |
| occurrences causally related to treatment / all      | 0 / 3          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Investigations                                       |                |  |  |
| Weight decreased                                     |                |  |  |
| subjects affected / exposed                          | 1 / 31 (3.23%) |  |  |
| occurrences causally related to treatment / all      | 0 / 1          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Injury, poisoning and procedural complications       |                |  |  |
| Fall                                                 |                |  |  |
| subjects affected / exposed                          | 2 / 31 (6.45%) |  |  |
| occurrences causally related to treatment / all      | 0 / 2          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Skin Laceration                                      |                |  |  |
| subjects affected / exposed                          | 2 / 31 (6.45%) |  |  |
| occurrences causally related to treatment / all      | 0 / 2          |  |  |
| deaths causally related to treatment / all           | 0 / 0          |  |  |
| Upper Limb Fracture                                  |                |  |  |

|                                                 |                |  |  |
|-------------------------------------------------|----------------|--|--|
| subjects affected / exposed                     | 1 / 31 (3.23%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Cardiac disorders                               |                |  |  |
| Cardiac failure                                 |                |  |  |
| subjects affected / exposed                     | 1 / 31 (3.23%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Cardiac Failure Congestive                      |                |  |  |
| subjects affected / exposed                     | 1 / 31 (3.23%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Myocardial Infarction                           |                |  |  |
| subjects affected / exposed                     | 1 / 31 (3.23%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Nervous system disorders                        |                |  |  |
| Cerebrovascular accident                        |                |  |  |
| subjects affected / exposed                     | 1 / 31 (3.23%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Encephalopathy                                  |                |  |  |
| subjects affected / exposed                     | 1 / 31 (3.23%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Spinal cord compression                         |                |  |  |
| subjects affected / exposed                     | 1 / 31 (3.23%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Syncope                                         |                |  |  |
| subjects affected / exposed                     | 1 / 31 (3.23%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Gastrointestinal disorders                      |                |  |  |

|                                                 |                |  |  |
|-------------------------------------------------|----------------|--|--|
| Vomiting                                        |                |  |  |
| subjects affected / exposed                     | 1 / 31 (3.23%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Oesophagitis                                    |                |  |  |
| subjects affected / exposed                     | 1 / 31 (3.23%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Nausea                                          |                |  |  |
| subjects affected / exposed                     | 1 / 31 (3.23%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Diarrhoea                                       |                |  |  |
| subjects affected / exposed                     | 2 / 31 (6.45%) |  |  |
| occurrences causally related to treatment / all | 0 / 2          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Renal and urinary disorders                     |                |  |  |
| Urinary retention                               |                |  |  |
| subjects affected / exposed                     | 1 / 31 (3.23%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Acute Kidney Injury                             |                |  |  |
| subjects affected / exposed                     | 1 / 31 (3.23%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Musculoskeletal and connective tissue disorders |                |  |  |
| Musculoskeletal Pain                            |                |  |  |
| subjects affected / exposed                     | 1 / 31 (3.23%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Infections and infestations                     |                |  |  |
| Lower respiratory tract infection               |                |  |  |

|                                                 |                |  |  |
|-------------------------------------------------|----------------|--|--|
| subjects affected / exposed                     | 1 / 31 (3.23%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Urinary tract infection                         |                |  |  |
| subjects affected / exposed                     | 1 / 31 (3.23%) |  |  |
| occurrences causally related to treatment / all | 1 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Metabolism and nutrition disorders              |                |  |  |
| Dehydration                                     |                |  |  |
| subjects affected / exposed                     | 1 / 31 (3.23%) |  |  |
| occurrences causally related to treatment / all | 0 / 1          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |

Frequency threshold for reporting non-serious adverse events: 0 %

|                                                       |                                                     |  |  |
|-------------------------------------------------------|-----------------------------------------------------|--|--|
| <b>Non-serious adverse events</b>                     | Abiraterone Acetate<br>+<br>Prednisone/Prednisolone |  |  |
| Total subjects affected by non-serious adverse events |                                                     |  |  |
| subjects affected / exposed                           | 0 / 31 (0.00%)                                      |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date          | Amendment                                                                                                                                                                                                                                                                                                                                                 |
|---------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 09 April 2012 | This amendment was created to incorporate the following changes: specified that this was a long-term safety follow-up study; updated follow-up for safety to a maximum of 3 years from the protocol issue date of 9 April 2012; added statement that consideration was given to extend the study duration following review of the safety data at 3 years. |
| 11 March 2015 | This amendment was created to incorporate the following changes: Updated the follow-up for safety to a maximum duration of 6 years from the protocol INT-1 issue date (9-April 2012); text updated to include current cytochrome (CYP)3A4 drug-drug interaction information.                                                                              |

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.

Site visits not conducted for prior studies. No CRF/clinical database generated. Most subjects lost follow-up due to disease. Data not collected per plan, noted per source notes, thus into CIOMS. Difficult to generalize results for small population.

Notes: