# Clinical trial results:
# Abiraterona acetate maintenance in combination with docetaxel after disease progression to abiraterona acetate in metastatic castration resistant prostate cancer. Randomized phase II study.

## Summary

| | |
|---|---|
| EudraCT number | 2013-003811-23 |
| Trial protocol | ES |
| Global end of trial date | 08 June 2020 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 16 October 2021 |
| First version publication date | 16 October 2021 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | ABIDO |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02036060 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | SOGUG - Spanish Oncology Genitourinary Group |
| Sponsor organisation address | Calle Velázquez, 7, planta 3, Madrid , Spain, 28001 |
| Public contact | Clinical Operations Department, APICES SOLUCIONES, S.L., +34 91 816 68 04 Ext 103, ana.moreno@apices.es |
| Scientific contact | Clinical Operations Department, APICES SOLUCIONES, S.L., +34 91 816 68 04 Ext103, ana.moreno@apices.es |

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 | 17 June 2021 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 08 June 2020 |
| Global end of trial reached? | Yes |
| Global end of trial date | 08 June 2020 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

12 months radiologic progression free survival of two arms of treatment (docetaxel + prednisone + abiraterone or docetaxel + prednisone) in metastatic castration resistant prostate cancer

Protection of trial subjects:

Randomization

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 03 February 2014 |
| 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 | Spain: 148 |
| Worldwide total number of subjects | 148 |
| EEA total number of subjects | 148 |

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) | 39 |
| From 65 to 84 years | 101 |
| 85 years and over | 8 |

## Subject disposition

### Recruitment

Recruitment details:

Patients were recruited in the study from 07th February 2014 until 27th July 2016.

Patients were randomised in the study from 30th July 2014 until 26th February 2019.

### Pre-assignment

Screening details:

Patients included in the study had had to show histologically or cytologically confirmed adenocarcinoma of the prostate, be asymptomatic or mildly symptomatic from prostate cancer, received previous anti-androgen therapy and progression after withdrawal, have a Life expectancy of at least 6 months, ECOG PS of 0-1 and adequate organ function.

### Pre-assignment period milestones

| | |
|---|---|
| Number of subjects started | 148 |
| Number of subjects completed | 94 |

### Pre-assignment subject non-completion reasons

| | |
|---|---|
| Reason: Number of subjects | Pre-randomisation loss (94 randomized): 54 |

### Period 1

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

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Arm A: Docetaxel + Prednisone + abiraterone |

Arm description:

Docetaxel 75 mg/m2 + prednisone 10 mg/d + abiraterone 1000 mg/d in 21 day cycles.

| | |
|---|---|
| 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:

4 tables of 250 mg/day (1000 mg)

| | |
|---|---|
| Investigational medicinal product name | Docetaxel |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate and solvent for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

75 mg/m2 every 21 days

| | |
|---|---|
| Investigational medicinal product name | Prednisone |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |

| | |
|---|---|
| Routes of administration | Oral use |

Dosage and administration details:

10 mg daily

| **Arm title** | Arm B: Docetaxel + Prednisone |
|---|---|

Arm description:

Docetaxel 75 mg/m2 plus prednisone 10 mg/d in 21 day cycles.

| | |
|---|---|
| Arm type | Active comparator |
| Investigational medicinal product name | Docetaxel |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate and solvent for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

75 mg/m2 every 21 days

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

Dosage and administration details:

10 mg daily

| **Number of subjects in period 1[1]** | Arm A: Docetaxel + Prednisone + abiraterone | Arm B: Docetaxel + Prednisone |
|---|---|---|
| Started | 47 | 47 |
| Completed | 22 | 20 |
| Not completed | 25 | 27 |
| Physician decision | 1 | - |
| Disease progression | 14 | 14 |
| Development of other intercurrent diseases | 1 | 4 |
| Unacceptable toxicity | 5 | 7 |
| Exitus | 4 | 2 |

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: During stage I of study, 148 patients were included. Prior to the start of Phase II, 54 patients were pre-randomisation failures, resulting in a total of 94 patients participating in stage II of the study.

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Arm A: Docetaxel + Prednisone + abiraterone |
| Reporting group description: | |
| Docetaxel 75 mg/m2 + prednisone 10 mg/d + abiraterone 1000 mg/d in 21 day cycles. | |
| Reporting group title | Arm B: Docetaxel + Prednisone |
| Reporting group description: | |
| Docetaxel 75 mg/m2 plus prednisone 10 mg/d in 21 day cycles. | |

| Reporting group values | Arm A: Docetaxel + Prednisone + abiraterone | Arm B: Docetaxel + Prednisone | Total |
|---|---|---|---|
| Number of subjects | 47 | 47 | 94 |
| Age categorical<br>Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 13 | 19 | 32 |
| From 65-84 years | 31 | 28 | 59 |
| 85 years and over | 3 | 0 | 3 |
| Age continuous<br>Units: years | | | |
| median | 70.0 | 68.0 | |
| full range (min-max) | 51.0 to 85.0 | 45.0 to 84.0 | - |
| Gender categorical<br>Units: Subjects | | | |
| Female | 0 | 0 | 0 |
| Male | 47 | 47 | 94 |
| Ethnics<br>Units: Subjects | | | |
| Caucasian | 46 | 46 | 92 |
| African | 0 | 1 | 1 |
| Arab | 1 | 0 | 1 |
| Risk behaviours: Tobacco<br>Units: Subjects | | | |
| Yes | 9 | 11 | 20 |
| No | 36 | 36 | 72 |
| Not available | 2 | 0 | 2 |
| Risk behaviours: Alcohol<br>Units: Subjects | | | |
| Yes | 3 | 9 | 12 |
| No | 42 | 38 | 80 |
| Not available | 2 | 0 | 2 |

| | | | |
|---|---|---|---|
| Intercurrent disease<br>Units: Subjects | | | |
| Yes | 41 | 40 | 81 |
| No | 6 | 7 | 13 |
| ECOG-PS<br>Units: Subjects | | | |
| 0) | 23 | 16 | 39 |
| 1) | 21 | 26 | 47 |
| 2) | 3 | 5 | 8 |
| TNM: Stage at initial diagnosis<br>Units: Subjects | | | |
| I) | 2 | 0 | 2 |
| II) | 7 | 4 | 11 |
| IIA) | 1 | 0 | 1 |
| III) | 11 | 7 | 18 |
| IV) | 22 | 26 | 48 |
| Not available | 4 | 10 | 14 |
| Gleason score at initial diagnosis<br>Units: Subjects | | | |
| <8 | 19 | 19 | 38 |
| ≥8 | 26 | 20 | 46 |
| Not available | 2 | 8 | 10 |
| Previous therapy: Radical prostatectomy<br>Units: Subjects | | | |
| Yes | 14 | 10 | 24 |
| No | 33 | 37 | 70 |
| Previous therapy: Radical radiotherapy<br>Units: Subjects | | | |
| Yes | 11 | 14 | 25 |
| No | 36 | 33 | 69 |
| Tumor location: Bone<br>Units: Subjects | | | |
| Yes | 40 | 40 | 80 |
| No | 7 | 7 | 14 |
| Tumor location: Lymph nodes<br>Units: Subjects | | | |
| Yes | 27 | 30 | 57 |
| No | 20 | 17 | 37 |
| Tumor location: Liver<br>Units: Subjects | | | |
| Yes | 4 | 4 | 8 |
| No | 43 | 43 | 86 |
| Number of locations per patient<br>Units: Subjects | | | |
| 1) | 22 | 17 | 39 |
| 2) | 18 | 19 | 37 |
| 3) | 5 | 6 | 11 |
| 4) | 1 | 3 | 4 |
| Non Evaluable | 1 | 2 | 3 |

| | | | |
|---|---|---|---|
| Height | | | |
| Units: Cm | | | |
| median | 168.3 | 169.0 | |
| full range (min-max) | 154.0 to 196.0 | 153.0 to 182.0 | - |
| Weight | | | |
| Units: Kg | | | |
| median | 79.3 | 82.0 | |
| full range (min-max) | 63.0 to 116.6 | 53.5 to 117.0 | - |
| Time since initial diagnosis | | | |
| Units: Months | | | |
| median | 48.8 | 39.6 | |
| full range (min-max) | 7.8 to 207.3 | 6.8 to 188.6 | - |
| Time since metastasic diagnosis | | | |
| Units: Months | | | |
| median | 11.7 | 14.9 | |
| full range (min-max) | 0.2 to 137.3 | 0.5 to 113.8 | - |
| Treatment duration of abiraterone phase I | | | |
| Units: Months | | | |
| median | 12.1 | 13.6 | |
| full range (min-max) | 2.6 to 60.0 | 2.8 to 39.9 | - |
| Number of cycles phase II | | | |
| Units: Cycles | | | |
| median | 8.0 | 8.0 | |
| full range (min-max) | 1.0 to 10.0 | 1.0 to 10.0 | - |
| Relative dose intensity of docetaxel | | | |
| Units: Percentage | | | |
| median | 87 | 87 | |
| full range (min-max) | 50 to 96 | 63 to 100 | - |
| Relative dose intensity of abiraterone phase II (only Arm A) | | | |
| Units: Percentage | | | |
| median | 94 | 0 | |
| full range (min-max) | 50 to 101 | 0 to 0 | - |
| PSA at baseline | | | |
| Units: ng/ml | | | |
| median | 73 | 34 | |
| full range (min-max) | 1 to 1401 | 0 to 4256 | - |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Arm A: Docetaxel + Prednisone + abiraterone |
| Reporting group description: | |
| Docetaxel 75 mg/m2 + prednisone 10 mg/d + abiraterone 1000 mg/d in 21 day cycles. | |
| Reporting group title | Arm B: Docetaxel + Prednisone |
| Reporting group description: | |
| Docetaxel 75 mg/m2 plus prednisone 10 mg/d in 21 day cycles. | |

### Primary: Radiological progression-free survival at 12 Months

| | |
|---|---|
| End point title | Radiological progression-free survival at 12 Months[1] |

End point description:

Radiological progression-free survival was defined as the time elapsed, in months, from the time the patient is randomised into the study until the patient progresses according to RECIST criteria and PCWG2 criteria or dies for any cause.

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

End point timeframe:

Every 12 weeks

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 statistical analyses have been performed. Phase II non-comparative study.

| End point values | Arm A: Docetaxel + Prednisone + abiraterone | Arm B: Docetaxel + Prednisone | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 47 | 47 | | |
| Units: Percentage | | | | |
| number (confidence interval 95%) | 34.9 (20.7 to 49.2) | 33.9 (19.5 to 48.3) | | |

| | |
|---|---|
| **Attachments (see zip file)** | rSLP.png |

### 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 elapsed, in months, from the time the patient was randomised into the study until death for any cause.

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

End point timeframe:

Every 12 weeks

| End point values | Arm A: Docetaxel + Prednisone + abiraterone | Arm B: Docetaxel + Prednisone | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 47 | 47 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 17.368 (14.058 to 20.679) | 16.908 (9.792 to 24.023) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Radiological progression-free survival of study arms

| End point title | Radiological progression-free survival of study arms |
|---|---|

End point description:

Radiological progression-free survival was defined as the time elapsed, in months, from the time the patient is randomised into the study until the patient progresses according to RECIST criteria and PCWG2 criteria or dies for any cause.

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

End point timeframe:

Every 12 weeks

| End point values | Arm A: Docetaxel + Prednisone + abiraterone | Arm B: Docetaxel + Prednisone | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 47 | 47 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 8.816 (5.948 to 11.684) | 9.770 (7.234 to 12.305) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: PSA progression free survival

| End point title | PSA progression free survival |
|---|---|

End point description:

PSA progression-free survival was defined as the time elapsed, in months, from the time the patient was randomised in the study until PSA progression, radiological progression or death for any cause.

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

End point timeframe:

Every 12 weeks

| **End point values** | Arm A: Docetaxel + Prednisone + abiraterone | Arm B: Docetaxel + Prednisone | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 47 | 47 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 5.428 (3.614 to 7.241) | 5.39 (4.003 to 5.928) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Biochemical response rate 50%

| End point title | Biochemical response rate 50% |
|---|---|

End point description:

Biochemical response has been defined as a reduction in PSA concentration of greater than 50% from the baseline stage II visit (first available determination prior to initiation of docetaxel treatment)

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

End point timeframe:

Everyb 4 weeks

| **End point values** | Arm A: Docetaxel + Prednisone + abiraterone | Arm B: Docetaxel + Prednisone | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 47 | 47 | | |
| Units: % of Subjects | | | | |
| Response | 64 | 47 | | |
| No response | 36 | 53 | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Biochemical response rate 90%

| End point title | Biochemical response rate 90% |
|---|---|

End point description:

Biochemical response has been defined as a reduction in PSA concentration of greater than 50% from the baseline stage II visit (first available determination prior to initiation of docetaxel treatment).

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

End point timeframe:

Every 4 weeks

| End point values | Arm A: Docetaxel + Prednisone + abiraterone | Arm B: Docetaxel + Prednisone | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 47 | 47 | | |
| Units: % of subjects | | | | |
| Response | 21 | 11 | | |
| No response | 79 | 89 | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Objective response rate

| End point title | Objective response rate |
|---|---|

End point description:

Objective response has been calculated taking into account patients which has been response to treatment. In this case, 7 patients of Arm A and 3 patients of Arm B had a partial response to treatment.

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

End point timeframe:

Every 12 weeks

| End point values | Arm A: Docetaxel + Prednisone + abiraterone | Arm B: Docetaxel + Prednisone | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 47 | 47 | | |
| Units: % of subjects | | | | |
| number (confidence interval 95%) | 14.9 (4.7 to 25.1) | 6.4 (0 to 13.4) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Mean change from baseline in the FACT-P total score (SD)b

| End point title | Mean change from baseline in the FACT-P total score (SD)b |
|---|---|

End point description:

The FACT-P scale includes 5 fields corresponding the following ranges: general physical status (range 0-28), family and social environment (range 0-28), emotional status (range 0-24), functioning ability (range 0-28) and prostate cancer specific symptoms (range 0-48); plus a total score (range 0-156). The higher the score, the better the quality of life.

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

End point timeframe:

Every 4 weeks

| End point values | Arm A: Docetaxel + Prednisone + abiraterone | Arm B: Docetaxel + Prednisone | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 26 | 31 | | |
| Units: Score | | | | |
| median (full range (min-max)) | -0.5 (-69.3 to 41.3) | -1.3 (-38.6 to 42.5) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Time to skeletal event

| End point title | Time to skeletal event |
|---|---|

End point description:

Time to skeletal event is defined has been defined as the time elapsed from randomization until the onset of skeletal event. The following were considered skeletal events: pathological fracture, spinal cord compression, radiotherapy or bone surgery, and hypercalcaemia of bone metastasis, occurring after randomisation in phase II. 9 patients (4 of Arm A and 5 of Arm B)shown skeletal events during stage II of the study.

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

End point timeframe:

Every 12 weeks.

| End point values | Arm A: Docetaxel + Prednisone + abiraterone | Arm B: Docetaxel + Prednisone | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 4 | 5 | | |
| Units: Months | | | | |
| median (full range (min-max)) | 1.2 (0.7 to 6.1) | 7.8 (4.0 to 8.9) | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Time to opiate initiation

| End point title | Time to opiate initiation |
|---|---|

End point description:

Time to opiate initiation was defined as the time elapsed, in months, from the patient was randomised in the study until opioide treatment initiation for oncologic pain. 35 patients (18 in arm A and 17 in arm B) started treatment with newly prescribed opioids. Four patients in both arms started opioid treatment on the same day they were randomised in stage II of the study.

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

End point timeframe:

Every 4 weeks

| End point values | Arm A: Docetaxel + Prednisone + abiraterone | Arm B: Docetaxel + Prednisone | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 18 | 17 | | |
| Units: Months | | | | |
| median (full range (min-max)) | 3.2 (0.0 to 14.7) | 1.4 (0.0 to 5.5) | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Worsening of pain according to BPI-SF

| End point title | Worsening of pain according to BPI-SF |
|---|---|

End point description:

Worsening of pain has been defined as an increase of at least 2 points, with respect to the lowest value measured during stage II, in item 3 of the BPI scale.

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

End point timeframe:

Every 4 weeks

| **End point values** | Arm A: Docetaxel + Prednisone + abiraterone | Arm B: Docetaxel + Prednisone | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 47 | 47 | | |
| Units: Patients | | | | |
| Yes | 25 | 26 | | |
| No | 22 | 21 | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

During phase II of study treatment (After randomization)

Adverse event reporting additional description:

Adverse events are shown in two groups depending on the treatment arm in which they occurred, differentiated as follows:

Arm A: Docetaxel + prednisone + Abiraterone.
Arm B: Docetaxel + prednisone

| | |
|---|---|
| Assessment type | Systematic |

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 23.1 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Arm A: Docetaxel + Prednisone + Abiraterone |
| Reporting group description: - | |
| Reporting group title | Arm B: Docetaxel + Prednisone |
| Reporting group description: - | |
| Reporting group title | Total |

Reporting group description: -

| Serious adverse events | Arm A: Docetaxel + Prednisone + Abiraterone | Arm B: Docetaxel + Prednisone | Total |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 31 / 47 (65.96%) | 20 / 47 (42.55%) | 51 / 94 (54.26%) |
| number of deaths (all causes) | 37 | 29 | 66 |
| number of deaths resulting from adverse events | 6 | 1 | 7 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Gastrointestinal stromal tumour | Additional description: Gastrointestinal stromal tumour grade 3 | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 47 (2.13%) | 1 / 94 (1.06%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Phlebitis | Additional description: Phlebitis grade 3 | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 47 (2.13%) | 1 / 94 (1.06%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Surgical and medical procedures | | | |
| Nephrostomy | Additional description: Nephrostomy grade 3 | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 47 (2.13%) | 1 / 94 (1.06%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Transurethral resection of bladder tumor | Additional description: Transurethral resection of bladder tumor grade 2 | | |
| subjects affected / exposed | 1 / 47 (2.13%) | 0 / 47 (0.00%) | 1 / 94 (1.06%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| General physical health deterioration | Additional description: 1 General physical health deterioration grade 4, 1 grade 3 and 1 grade 2.<br>General physical health deterioration grade 4 related with docetaxel. General physical health deterioration grade 3 related with abidaterone. | | |
| subjects affected / exposed | 3 / 47 (6.38%) | 0 / 47 (0.00%) | 3 / 94 (3.19%) |
| occurrences causally related to treatment / all | 2 / 3 | 0 / 0 | 2 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General body pain | Additional description: General body pain grade 3 | | |
| subjects affected / exposed | 1 / 47 (2.13%) | 0 / 47 (0.00%) | 1 / 94 (1.06%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fever | Additional description: Fever grade 1 related with abiraterone | | |
| subjects affected / exposed | 1 / 47 (2.13%) | 0 / 47 (0.00%) | 1 / 94 (1.06%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mucositis | Additional description: Mucositis grade 3 related with docetaxel | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 47 (2.13%) | 1 / 94 (1.06%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute respiratory insufficiency | Additional description: Acute respiratory insufficiency grade 5 | | |
| subjects affected / exposed | 1 / 47 (2.13%) | 0 / 47 (0.00%) | 1 / 94 (1.06%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| Chronic obstructive pulmonary disease exacerbation | Additional description: 2 Chronic obstructive pulmonary disease exacerbation grade 3 | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 47 (0.00%) | 2 / 47 (4.26%) | 2 / 94 (2.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| Neutrophil count decreased | Additional description: Neutrophil count decreased grade 4 related with docetaxel | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 47 (2.13%) | 1 / 94 (1.06%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| GGT increased | Additional description: GGT increased grade 4 | | |
| subjects affected / exposed | 1 / 47 (2.13%) | 0 / 47 (0.00%) | 1 / 94 (1.06%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Hip fracture | Additional description: 2 Hip fracture grade 3 | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 2 / 47 (4.26%) | 2 / 94 (2.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rib fracture | Additional description: Rib fracture grade 2 | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 47 (2.13%) | 1 / 94 (1.06%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung injury | Additional description: Lung injury grade 3 | | |
| subjects affected / exposed | 1 / 47 (2.13%) | 0 / 47 (0.00%) | 1 / 94 (1.06%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Acute cardiac event | Additional description: Acute cardiac event grade 5 related with abidaterone and docetaxel | | |
| subjects affected / exposed | 1 / 47 (2.13%) | 0 / 47 (0.00%) | 1 / 94 (1.06%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| Cardiac failure congestive | Additional description: Cardiac failure congestive grade 3 related with abiraterone and docetaxel | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 47 (2.13%) | 0 / 47 (0.00%) | 1 / 94 (1.06%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Brain stem stroke | Additional description: Brain stem stroke Grade 5 | | |
| subjects affected / exposed | 1 / 47 (2.13%) | 0 / 47 (0.00%) | 1 / 94 (1.06%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| Spinal cord compression | Additional description: 1 Spinal cord compression Grade 3 and 1 Grade 5 | | |
| subjects affected / exposed | 2 / 47 (4.26%) | 0 / 47 (0.00%) | 2 / 94 (2.13%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| Hepatic encephalopathy | Additional description: Hepatic encephalopathy grade 4 related with docetaxel | | |
| subjects affected / exposed | 1 / 47 (2.13%) | 0 / 47 (0.00%) | 1 / 94 (1.06%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | Additional description: Anaemia Grade 4 | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 47 (2.13%) | 1 / 94 (1.06%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Leukopenia | Additional description: 2 Leukopenia grade 4 related with docetaxel | | |
| subjects affected / exposed | 1 / 47 (2.13%) | 1 / 47 (2.13%) | 2 / 94 (2.13%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neutropenia | Additional description: 2 Neutropenia grade 3 (1 in Arm A and 1 in Arm B) and 20 grade 4 (18 in Arm A and 2 in Arm B). All related with docetaxel and one of them with abiraterone | | |
| subjects affected / exposed | 19 / 47 (40.43%) | 3 / 47 (6.38%) | 22 / 94 (23.40%) |
| occurrences causally related to treatment / all | 19 / 19 | 3 / 3 | 22 / 22 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Febrile neutropenia | Additional description: 8 febrile neutropenia grade 3 (2 in Arm A and 6 in Arm B) and 7 grade 4 (6 in Arm A and 1 in Arm B), all related with docetaxel. | | |
| subjects affected / exposed | 8 / 47 (17.02%) | 7 / 47 (14.89%) | 15 / 94 (15.96%) |
| occurrences causally related to treatment / all | 8 / 8 | 7 / 7 | 15 / 15 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---|---|---|
| Gastrointestinal disorders | | | |
| Diarrhoea | Additional description: 2 diarrohoea grade 3 related with docetaxel. | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 2 / 47 (4.26%) | 2 / 94 (2.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 2 / 2 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Enteritis leukopenic | Additional description: Enteritis leukopenic grade 4 related with docetaxel | | |
| subjects affected / exposed | 1 / 47 (2.13%) | 0 / 47 (0.00%) | 1 / 94 (1.06%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Constipation | Additional description: Constipation grade 3 | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 47 (2.13%) | 1 / 94 (1.06%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mesenteric ischemia | Additional description: Mesenteric ischemia grade 5 related with docetaxel | | |
| subjects affected / exposed | 1 / 47 (2.13%) | 0 / 47 (0.00%) | 1 / 94 (1.06%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| Renal and urinary disorders | | | |
| Hematuria | Additional description: 5 Hematuria grade 3 | | |
| subjects affected / exposed | 4 / 47 (8.51%) | 1 / 47 (2.13%) | 5 / 94 (5.32%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 1 | 0 / 5 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Insufficiency renal | Additional description: Insufficiency renal grade 3 | | |
| subjects affected / exposed | 1 / 47 (2.13%) | 0 / 47 (0.00%) | 1 / 94 (1.06%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Knee arthritis | Additional description: Knee arthritis Grade 3 | | |
| subjects affected / exposed | 1 / 47 (2.13%) | 0 / 47 (0.00%) | 1 / 94 (1.06%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lumbar pain | Additional description: Lumbar pain grade 3 | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 47 (2.13%) | 1 / 94 (1.06%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bone pain | Additional description: Bone pain grade 3 | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 47 (2.13%) | 1 / 94 (1.06%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pelvic bone pain | Additional description: Pelvic bone pain grade 3 | | |
| subjects affected / exposed | 1 / 47 (2.13%) | 0 / 47 (0.00%) | 1 / 94 (1.06%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Influenza A virus infection | Additional description: Influenza A virus infection grade 3 | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 1 / 47 (2.13%) | 1 / 94 (1.06%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory infection | Additional description: 2 Respiratory infection grade 3 | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 2 / 47 (4.26%) | 2 / 94 (2.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower respiratory tract infection | Additional description: 2 Lower respiratory tract infection grade 3 | | |
| subjects affected / exposed | 1 / 47 (2.13%) | 1 / 47 (2.13%) | 2 / 94 (2.13%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection | Additional description: 1 Urinary tract infection grade 3 and 1 grade 2 | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 2 / 47 (4.26%) | 2 / 94 (2.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary infection | Additional description: 2 Urinary infection grade 3 | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 2 / 47 (4.26%) | 2 / 94 (2.13%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | Additional description: 3 Pneumonia grade 3, 1 related with docetaxel | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 3 / 47 (6.38%) | 0 / 47 (0.00%) | 3 / 94 (3.19%) |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 0 | 1 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sepsis | Additional description: 1 Sepsis grade 3 (Arm A) and 1 grade 4 (Arm B). Sepsis grade 4 related with docetaxel. | | |
| subjects affected / exposed | 1 / 47 (2.13%) | 1 / 47 (2.13%) | 2 / 94 (2.13%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Clostridial sepsis | Additional description: Clostridial sepsis grade 3 related with docetaxel | | |
| subjects affected / exposed | 1 / 47 (2.13%) | 0 / 47 (0.00%) | 1 / 94 (1.06%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urosepsis | Additional description: Urosepsis grade 2 | | |
| subjects affected / exposed | 1 / 47 (2.13%) | 0 / 47 (0.00%) | 1 / 94 (1.06%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Septic shock | Additional description: 1 Septic shock grade 3 (Arm A) and 2 grade 5 (1 in Arm A and 1 in Arm B). 1 shock septic grade 5 (Arm A) related with docetaxel. | | |
| subjects affected / exposed | 2 / 47 (4.26%) | 1 / 47 (2.13%) | 3 / 94 (3.19%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 1 | 1 / 3 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 1 | 1 / 2 |
| Metabolism and nutrition disorders | | | |
| Fluid retention | Additional description: Fluid retention grade 3 related with docetaxel | | |
| subjects affected / exposed | 1 / 47 (2.13%) | 0 / 47 (0.00%) | 1 / 94 (1.06%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

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

| **Non-serious adverse events** | Arm A: Docetaxel + Prednisone + Abiraterone | Arm B: Docetaxel + Prednisone | Total |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 47 / 47 (100.00%) | 44 / 47 (93.62%) | 91 / 94 (96.81%) |
| Vascular disorders | | | |
| Hypertension | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 3 / 47 (6.38%) | 4 / 47 (8.51%) | 7 / 94 (7.45%) |
| occurrences (all) | 6 | 5 | 11 |
| Hypotension | | | |
| subjects affected / exposed | 4 / 47 (8.51%) | 1 / 47 (2.13%) | 5 / 94 (5.32%) |
| occurrences (all) | 6 | 2 | 8 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 37 / 47 (78.72%) | 34 / 47 (72.34%) | 71 / 94 (75.53%) |
| occurrences (all) | 94 | 83 | 177 |
| General physical health deterioration | | | |
| subjects affected / exposed | 4 / 47 (8.51%) | 0 / 47 (0.00%) | 4 / 94 (4.26%) |
| occurrences (all) | 4 | 0 | 4 |
| Pain | | | |
| subjects affected / exposed | 5 / 47 (10.64%) | 3 / 47 (6.38%) | 8 / 94 (8.51%) |
| occurrences (all) | 6 | 4 | 10 |
| Thoracic pain | | | |
| subjects affected / exposed | 3 / 47 (6.38%) | 0 / 47 (0.00%) | 3 / 94 (3.19%) |
| occurrences (all) | 3 | 0 | 3 |
| Oedema | | | |
| subjects affected / exposed | 7 / 47 (14.89%) | 0 / 47 (0.00%) | 7 / 94 (7.45%) |
| occurrences (all) | 8 | 0 | 8 |
| Oedema peripheral | | | |
| subjects affected / exposed | 11 / 47 (23.40%) | 6 / 47 (12.77%) | 17 / 94 (18.09%) |
| occurrences (all) | 13 | 6 | 19 |
| Fatigue | | | |
| subjects affected / exposed | 3 / 47 (6.38%) | 0 / 47 (0.00%) | 3 / 94 (3.19%) |
| occurrences (all) | 6 | 0 | 6 |
| Mucosal inflammation | | | |
| subjects affected / exposed | 13 / 47 (27.66%) | 11 / 47 (23.40%) | 24 / 94 (25.53%) |
| occurrences (all) | 17 | 16 | 33 |
| Pyrexia | | | |
| subjects affected / exposed | 12 / 47 (25.53%) | 9 / 47 (19.15%) | 21 / 94 (22.34%) |
| occurrences (all) | 13 | 11 | 24 |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | |
|---|---|---|---|
| Catarrh | | | |
| subjects affected / exposed | 4 / 47 (8.51%) | 1 / 47 (2.13%) | 5 / 94 (5.32%) |
| occurrences (all) | 4 | 2 | 6 |
| Dyspnoea | | | |
| subjects affected / exposed | 6 / 47 (12.77%) | 1 / 47 (2.13%) | 7 / 94 (7.45%) |
| occurrences (all) | 7 | 1 | 8 |
| Cough | | | |
| subjects affected / exposed | 4 / 47 (8.51%) | 3 / 47 (6.38%) | 7 / 94 (7.45%) |
| occurrences (all) | 5 | 5 | 10 |
| Psychiatric disorders | | | |
| Insomnia | | | |
| subjects affected / exposed | 2 / 47 (4.26%) | 4 / 47 (8.51%) | 6 / 94 (6.38%) |
| occurrences (all) | 2 | 4 | 6 |
| Investigations | | | |
| Blood creatinine increased | | | |
| subjects affected / exposed | 1 / 47 (2.13%) | 3 / 47 (6.38%) | 4 / 94 (4.26%) |
| occurrences (all) | 5 | 8 | 13 |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 8 / 47 (17.02%) | 5 / 47 (10.64%) | 13 / 94 (13.83%) |
| occurrences (all) | 9 | 11 | 20 |
| Nervous system disorders | | | |
| Dysgeusia | | | |
| subjects affected / exposed | 8 / 47 (17.02%) | 13 / 47 (27.66%) | 21 / 94 (22.34%) |
| occurrences (all) | 12 | 17 | 29 |
| Dizziness | | | |
| subjects affected / exposed | 2 / 47 (4.26%) | 4 / 47 (8.51%) | 6 / 94 (6.38%) |
| occurrences (all) | 2 | 4 | 6 |
| Neuropathy peripheral | | | |
| subjects affected / exposed | 7 / 47 (14.89%) | 7 / 47 (14.89%) | 14 / 94 (14.89%) |
| occurrences (all) | 11 | 9 | 20 |
| Peripheral sensory neuropathy | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 4 / 47 (8.51%) | 4 / 94 (4.26%) |
| occurrences (all) | 0 | 6 | 6 |
| Neurotoxicity | | | |
| subjects affected / exposed | 4 / 47 (8.51%) | 9 / 47 (19.15%) | 13 / 94 (13.83%) |
| occurrences (all) | 5 | 10 | 15 |
| Paresthesia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 6 / 47 (12.77%) | 4 / 47 (8.51%) | 10 / 94 (10.64%) |
| occurrences (all) | 12 | 6 | 18 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 13 / 47 (27.66%) | 8 / 47 (17.02%) | 21 / 94 (22.34%) |
| occurrences (all) | 24 | 12 | 36 |
| Leukopenia | | | |
| subjects affected / exposed | 0 / 47 (0.00%) | 3 / 47 (6.38%) | 3 / 94 (3.19%) |
| occurrences (all) | 0 | 3 | 3 |
| Neutropenia | | | |
| subjects affected / exposed | 18 / 47 (38.30%) | 16 / 47 (34.04%) | 34 / 94 (36.17%) |
| occurrences (all) | 28 | 19 | 47 |
| Febrile neutropenia | | | |
| subjects affected / exposed | 8 / 47 (17.02%) | 6 / 47 (12.77%) | 14 / 94 (14.89%) |
| occurrences (all) | 8 | 6 | 14 |
| Eye disorders | | | |
| Excess tears | | | |
| subjects affected / exposed | 9 / 47 (19.15%) | 4 / 47 (8.51%) | 13 / 94 (13.83%) |
| occurrences (all) | 10 | 5 | 15 |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 26 / 47 (55.32%) | 24 / 47 (51.06%) | 50 / 94 (53.19%) |
| occurrences (all) | 46 | 67 | 113 |
| Abdominal pain | | | |
| subjects affected / exposed | 5 / 47 (10.64%) | 2 / 47 (4.26%) | 7 / 94 (7.45%) |
| occurrences (all) | 8 | 4 | 12 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 3 / 47 (6.38%) | 2 / 47 (4.26%) | 5 / 94 (5.32%) |
| occurrences (all) | 3 | 2 | 5 |
| Constipation | | | |
| subjects affected / exposed | 14 / 47 (29.79%) | 12 / 47 (25.53%) | 26 / 94 (27.66%) |
| occurrences (all) | 25 | 15 | 40 |
| Nausea | | | |
| subjects affected / exposed | 12 / 47 (25.53%) | 12 / 47 (25.53%) | 24 / 94 (25.53%) |
| occurrences (all) | 17 | 25 | 42 |
| Vomiting | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 5 / 47 (10.64%) | 8 / 47 (17.02%) | 13 / 94 (13.83%) |
| occurrences (all) | 7 | 13 | 20 |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia | | | |
| subjects affected / exposed | 19 / 47 (40.43%) | 19 / 47 (40.43%) | 38 / 94 (40.43%) |
| occurrences (all) | 32 | 22 | 54 |
| Nail dystrophy | | | |
| subjects affected / exposed | 5 / 47 (10.64%) | 3 / 47 (6.38%) | 8 / 94 (8.51%) |
| occurrences (all) | 5 | 4 | 9 |
| Erythema | | | |
| subjects affected / exposed | 3 / 47 (6.38%) | 4 / 47 (8.51%) | 7 / 94 (7.45%) |
| occurrences (all) | 3 | 4 | 7 |
| Eruption | | | |
| subjects affected / exposed | 3 / 47 (6.38%) | 2 / 47 (4.26%) | 5 / 94 (5.32%) |
| occurrences (all) | 3 | 2 | 5 |
| Onycholysis | | | |
| subjects affected / exposed | 6 / 47 (12.77%) | 4 / 47 (8.51%) | 10 / 94 (10.64%) |
| occurrences (all) | 10 | 5 | 15 |
| Pruritus | | | |
| subjects affected / exposed | 1 / 47 (2.13%) | 3 / 47 (6.38%) | 4 / 94 (4.26%) |
| occurrences (all) | 1 | 5 | 6 |
| Skin toxicity | | | |
| subjects affected / exposed | 3 / 47 (6.38%) | 3 / 47 (6.38%) | 6 / 94 (6.38%) |
| occurrences (all) | 4 | 6 | 10 |
| Nail disorder | | | |
| subjects affected / exposed | 8 / 47 (17.02%) | 7 / 47 (14.89%) | 15 / 94 (15.96%) |
| occurrences (all) | 15 | 13 | 28 |
| Renal and urinary disorders | | | |
| Hematuria | | | |
| subjects affected / exposed | 2 / 47 (4.26%) | 3 / 47 (6.38%) | 5 / 94 (5.32%) |
| occurrences (all) | 5 | 4 | 9 |
| Urinary retention | | | |
| subjects affected / exposed | 3 / 47 (6.38%) | 2 / 47 (4.26%) | 5 / 94 (5.32%) |
| occurrences (all) | 3 | 2 | 5 |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|---|---|---|---|
| Arthralgia | | | |
| subjects affected / exposed | 9 / 47 (19.15%) | 10 / 47 (21.28%) | 19 / 94 (20.21%) |
| occurrences (all) | 12 | 13 | 25 |
| Back pain | | | |
| subjects affected / exposed | 15 / 47 (31.91%) | 11 / 47 (23.40%) | 26 / 94 (27.66%) |
| occurrences (all) | 23 | 15 | 38 |
| Pain in extremity | | | |
| subjects affected / exposed | 8 / 47 (17.02%) | 6 / 47 (12.77%) | 14 / 94 (14.89%) |
| occurrences (all) | 10 | 8 | 18 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 7 / 47 (14.89%) | 7 / 47 (14.89%) | 14 / 94 (14.89%) |
| occurrences (all) | 13 | 10 | 23 |
| Bone pain | | | |
| subjects affected / exposed | 3 / 47 (6.38%) | 4 / 47 (8.51%) | 7 / 94 (7.45%) |
| occurrences (all) | 4 | 5 | 9 |
| Muscle spasms | | | |
| subjects affected / exposed | 3 / 47 (6.38%) | 0 / 47 (0.00%) | 3 / 94 (3.19%) |
| occurrences (all) | 3 | 0 | 3 |
| Myalgia | | | |
| subjects affected / exposed | 6 / 47 (12.77%) | 4 / 47 (8.51%) | 10 / 94 (10.64%) |
| occurrences (all) | 7 | 6 | 13 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 17 / 47 (36.17%) | 9 / 47 (19.15%) | 26 / 94 (27.66%) |
| occurrences (all) | 26 | 14 | 40 |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 16 June 2015 | Amendment 1: Protocol Vs 2.0 |
| 11 November 2019 | Amendment 7: Protocol Vs 3.0 |
| 13 April 2020 | Amendment 8: Protocol Vs 4.0 |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported