



Clinical trial results:

A Phase III, Open Label, Randomized Study to Assess the Efficacy and Safety of Olaparib (Lynparza™) Versus Enzalutamide or Abiraterone Acetate in Men with Metastatic Castration-Resistant Prostate Cancer Who Have Failed Prior Treatment with a New Hormonal Agent and Have Homologous Recombination Repair Gene Mutations (PROfound)

Summary

| | |
|--------------------------|----------------------|
| EudraCT number | 2016-000300-28 |
| Trial protocol | SE DK NO ES AT FR IT |
| Global end of trial date | 20 March 2020 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v1 (current) |
| This version publication date | 21 October 2023 |
| First version publication date | 21 October 2023 |

Trial information

Trial identification

| | |
|-----------------------|-------------|
| Sponsor protocol code | D081DC00007 |
|-----------------------|-------------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | AstraZeneca Clinical Study Information Center |
| Sponsor organisation address | Melbourn Science Park, Royston, United Kingdom, SG8 6EE |
| Public contact | Global Clinical Lead, AstraZeneca Clinical Study Information Center, +1 8772409479, information.center@astrazeneca.com |
| Scientific contact | Global Clinical Lead, AstraZeneca Clinical Study Information Center, +1 8772409479, information.center@astrazeneca.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 | 20 March 2020 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 20 March 2020 |
| Global end of trial reached? | Yes |
| Global end of trial date | 20 March 2020 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary endpoint of the study is radiographic progression free survival (rPFS) in subjects with BRCA1, BRCA2 or ATM mutations (Cohort A).

Protection of trial subjects:

Patients given full and adequate oral and written information about the nature, purpose, possible risk and benefit of the study.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 06 February 2017 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|--|
| Country: Number of subjects enrolled | France: 62 |
| Country: Number of subjects enrolled | Japan: 57 |
| Country: Number of subjects enrolled | Canada: 32 |
| Country: Number of subjects enrolled | Turkey: 30 |
| Country: Number of subjects enrolled | Australia: 24 |
| Country: Number of subjects enrolled | Korea, Democratic People's Republic of: 29 |
| Country: Number of subjects enrolled | Netherlands: 21 |
| Country: Number of subjects enrolled | United States: 33 |
| Country: Number of subjects enrolled | Italy: 15 |
| Country: Number of subjects enrolled | Taiwan: 15 |
| Country: Number of subjects enrolled | Brazil: 14 |
| Country: Number of subjects enrolled | Argentina: 9 |
| Country: Number of subjects enrolled | Israel: 9 |
| Country: Number of subjects enrolled | Germany: 12 |
| Country: Number of subjects enrolled | Spain: 9 |
| Country: Number of subjects enrolled | Sweden: 2 |
| Country: Number of subjects enrolled | United Kingdom: 4 |
| Country: Number of subjects enrolled | Austria: 6 |
| Country: Number of subjects enrolled | Denmark: 1 |
| Country: Number of subjects enrolled | Norway: 3 |

| | |
|------------------------------------|-----|
| Worldwide total number of subjects | 387 |
| EEA total number of subjects | 131 |

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) | 116 |
| From 65 to 84 years | 260 |
| 85 years and over | 11 |

Subject disposition

Recruitment

Recruitment details:

Subjects were divided into two cohorts based on HRR gene mutation status. Subjects with mutations in either BRCA1, BRCA2, or ATM are in Cohort A whereas subjects with mutations among 12 other genes involved in the HRR pathway (BARD1, BRIP1, CDK12, CHEK1, CHEK2, FANCL, PALB2, PPP2R2A, RAD51B, RAD51C, RAD51D, or RAD54L) are in Cohort B.

Pre-assignment

Screening details:

Consenting subjects were assessed to ensure they met eligibility criteria.

Period 1

| | |
|------------------------------|---|
| Period 1 title | Overall Study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Carer, Assessor |

Arms

| | |
|------------------------------|----------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Cohort A Olaparib 300mg bd |

Arm description:

2x150mg film-coated tablets

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

Dosage and administration details:

300mg twice daily (100mg and 150mg tablets)

| | |
|------------------|--------------------------------------|
| Arm title | Cohort A Investigators choice of NHA |
|------------------|--------------------------------------|

Arm description:

either enzalutamide capsules (160 mg od) or abiraterone acetate tablets (1,000 mg od with 5 mg bid prednisone)

| | |
|--|-------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Enzalutamide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

160mg once daily (40mg tablets)

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

Dosage and administration details:

1000mg once daily (250mg or 500mg tablets) with prednisone 5mg bd

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

Dosage and administration details:

5mg bd with abiraterone acetate 1000mg od. Prednisolone was permitted for use instead of prednisone

| | |
|------------------|----------------------------|
| Arm title | Cohort B Olaparib 300mg bd |
|------------------|----------------------------|

Arm description:

2x150mg film-coated tablets

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

Dosage and administration details:

300mg twice daily (100mg and 150mg tablets)

| | |
|------------------|--------------------------------------|
| Arm title | Cohort B Investigators choice of NHA |
|------------------|--------------------------------------|

Arm description:

either enzalutamide capsules (160 mg od) or abiraterone acetate tablets (1,000 mg od with 5 mg bid prednisone)

| | |
|--|-------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Enzalutamide |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

160mg once daily (40mg tablets)

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

Dosage and administration details:

5mg bd with abiraterone acetate 1000mg od. Prednisolone was permitted for use instead of prednisone

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

Dosage and administration details:

1000mg once daily (250mg or 500mg tablets) with prednisone 5mg bd

| Number of subjects in period 1 | Cohort A Olaparib 300mg bd | Cohort A Investigators choice of NHA | Cohort B Olaparib 300mg bd |
|--------------------------------|-------------------------------|--|-------------------------------|
| | | | |
| Started | 162 | 83 | 94 |
| Completed | 0 | 0 | 0 |
| Not completed | 162 | 83 | 94 |
| Adverse event, serious fatal | 88 | 54 | 67 |
| Consent withdrawn by subject | 21 | 7 | 7 |
| Disease progression | - | - | - |
| Ongoing study at data cut off | 49 | 21 | 19 |
| Study terminated by sponsor | 1 | - | - |
| Investigator decision | - | 1 | - |
| Screen failure | - | - | - |
| Lost to follow-up | 3 | - | 1 |

| Number of subjects in period 1 | Cohort B Investigators choice of NHA |
|--------------------------------|--|
| Started | 48 |
| Completed | 0 |
| Not completed | 48 |
| Adverse event, serious fatal | 28 |
| Consent withdrawn by subject | 6 |
| Disease progression | 1 |
| Ongoing study at data cut off | 12 |
| Study terminated by sponsor | - |
| Investigator decision | - |
| Screen failure | 1 |
| Lost to follow-up | - |

Baseline characteristics

Reporting groups

| | |
|--|--------------------------------------|
| Reporting group title | Cohort A Olaparib 300mg bd |
| Reporting group description: | |
| 2x150mg film-coated tablets | |
| Reporting group title | Cohort A Investigators choice of NHA |
| Reporting group description: | |
| either enzalutamide capsules (160 mg od) or abiraterone acetate tablets (1,000 mg od with 5 mg bid prednisone) | |
| Reporting group title | Cohort B Olaparib 300mg bd |
| Reporting group description: | |
| 2x150mg film-coated tablets | |
| Reporting group title | Cohort B Investigators choice of NHA |
| Reporting group description: | |
| either enzalutamide capsules (160 mg od) or abiraterone acetate tablets (1,000 mg od with 5 mg bid prednisone) | |

| Reporting group values | Cohort A Olaparib 300mg bd | Cohort A Investigators choice of NHA | Cohort B Olaparib 300mg bd |
|---|-------------------------------|--|-------------------------------|
| Number of subjects | 162 | 83 | 94 |
| Age categorical 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) | 54 | 23 | 28 |
| From 65-84 years | 105 | 59 | 64 |
| 85 years and over | 3 | 1 | 2 |
| Age Continuous Units: Years | | | |
| arithmetic mean | 68.0 | 68.1 | 69.2 |
| standard deviation | ± 8.23 | ± 7.36 | ± 8.79 |
| Sex: Female, Male Units: Participants | | | |
| Female | 0 | 0 | 0 |
| Male | 162 | 83 | 94 |
| Race/Ethnicity, Customized Units: Subjects | | | |
| White | 109 | 55 | 54 |
| Black or African American | 2 | 1 | 5 |
| Asian | 43 | 19 | 26 |
| Other | 1 | 1 | 1 |
| Missing | 7 | 7 | 8 |

| Reporting group values | Cohort B Investigators choice of NHA | Total | |
|---|--|-------|--|
| Number of subjects | 48 | 387 | |
| Age categorical 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) | 11 | 116 | |
| From 65-84 years | 35 | 263 | |
| 85 years and over | 2 | 8 | |
| Age Continuous Units: Years | | | |
| arithmetic mean | 70.3 | | |
| standard deviation | ± 7.83 | - | |
| Sex: Female, Male Units: Participants | | | |
| Female | 0 | 0 | |
| Male | 48 | 387 | |
| Race/Ethnicity, Customized Units: Subjects | | | |
| White | 30 | 248 | |
| Black or African American | 0 | 8 | |
| Asian | 17 | 105 | |
| Other | 0 | 3 | |
| Missing | 1 | 23 | |

End points

End points reporting groups

| | |
|--|--|
| Reporting group title | Cohort A Olaparib 300mg bd |
| Reporting group description: 2x150mg film-coated tablets | |
| Reporting group title | Cohort A Investigators choice of NHA |
| Reporting group description: either enzalutamide capsules (160 mg od) or abiraterone acetate tablets (1,000 mg od with 5 mg bid prednisone) | |
| Reporting group title | Cohort B Olaparib 300mg bd |
| Reporting group description: 2x150mg film-coated tablets | |
| Reporting group title | Cohort B Investigators choice of NHA |
| Reporting group description: either enzalutamide capsules (160 mg od) or abiraterone acetate tablets (1,000 mg od with 5 mg bid prednisone) | |
| Subject analysis set title | Cohort A+B Olaparib 300mg bd |
| Subject analysis set type | Full analysis |
| Subject analysis set description: Subjects with HRR qualifying mutations (Cohort A+B) | |
| Subject analysis set title | Cohort A+B Investigators Choice of NHA |
| Subject analysis set type | Full analysis |
| Subject analysis set description: Subjects with HRR qualifying mutations (Cohort A+B) | |

Primary: Radiological Progression Free Survival (rPFS) by blinded independent central review (BICR) - Cohort A only

| | |
|---|---|
| End point title | Radiological Progression Free Survival (rPFS) by blinded independent central review (BICR) - Cohort A only ^[1] |
| End point description: The time from randomisation until the date of objective radiological disease progression (determined by RECIST 1.1 (soft tissue) and Prostate Cancer Working Group 3 (PCWG-3) (bone)) or death (by any cause in the absence of progression) regardless of whether the patient withdrew from randomised therapy or received another anti-cancer therapy prior to progression. Progression is defined using (i) Response Evaluation Criteria In Solid Tumors Criteria (RECIST v1.1) for soft tissue, as a $\geq 20\%$ increase in the sum of diameters of target lesions and an absolute increase of $\geq 5\text{mm}$ taking as reference the smallest sum of diameters since treatment started including the baseline sum of diameters; (ii) Prostate Cancer Working Group 3 (PGWG-3) for bone as ≥ 2 new bone lesions on the 1st week 8 scan compared to baseline. The confirmatory scan, ≥ 6 weeks later, must show ≥ 2 more new bone lesions (for a total of ≥ 4 new bone lesions since baseline). | |
| End point type | Primary |
| End point timeframe: Tumor assessments every 8 weeks from randomisation until radiographic progression assessed by BICR (median duration of treatment of 7 and 4 months for Olaparib and Investigators Choice of NHA respectively). | |

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The study was designed to formally test these endpoints in only Cohort A patients, there is just 1 endpoint that is formally tested for both Cohort A and Cohort B which is rPFS. All other analyses are descriptive only

| End point values | Cohort A Olaparib 300mg bd | Cohort A Investigators choice of NHA | | |
|----------------------------------|----------------------------------|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 162 | 83 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 7.39 (6.24 to 9.33) | 3.55 (1.91 to 3.71) | | |

Statistical analyses

| Statistical analysis title | Primary analysis |
|--|---|
| Statistical analysis description: | |
| Radiological Progression Free Survival (rPFS) by blinded independent central review (BICR) | |
| Comparison groups | Cohort A Olaparib 300mg bd v Cohort A Investigators choice of NHA |
| Number of subjects included in analysis | 245 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[2] |
| P-value | < 0.0001 ^[3] |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.34 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.25 |
| upper limit | 0.47 |

Notes:

[2] - Cohort A

[3] - 2-sided

Secondary: Confirmed Objective Response Rate (ORR) by blinded independent central review (BICR) - Cohort A only

| | |
|-----------------|---|
| End point title | Confirmed Objective Response Rate (ORR) by blinded independent central review (BICR) - Cohort A only ^[4] |
|-----------------|---|

End point description:

ORR is the percentage of patients with at least one visit response of Complete response (CR) or Partial response (PR), in their soft tissue disease assessed by Response Evaluation Criteria In Solid Tumors Criteria (RECIST v1.1), in the absence of progression on bone scan assessed by Prostate Cancer Working Group 3 (PCWG3)). Per RECIST v1.1, CR=Disappearance of all target lesions; PR = $\geq 30\%$ decrease in the sum of diameters of target lesions; For each treatment group, ORR is the number of patients with a CR and PR.

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

End point timeframe:

Tumor assessments every 8 weeks from randomisation until radiographic progression assessed by BICR (median duration of treatment of 7 and 4 months for Olaparib and Investigators Choice of NHA respectively).

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The study was designed to formally test these endpoints in only Cohort A patients, there is just 1 endpoint that is formally tested for both Cohort A and Cohort B which is rPFS. All other analyses are descriptive only

| End point values | Cohort A Olaparib 300mg bd | Cohort A Investigators choice of NHA | | |
|-----------------------------|----------------------------------|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 84 | 43 | | |
| Units: Participants | | | | |
| Response | 28 | 1 | | |
| No response | 56 | 42 | | |

Statistical analyses

| Statistical analysis title | Secondary analysis |
|---|---|
| Comparison groups | Cohort A Olaparib 300mg bd v Cohort A Investigators choice of NHA |
| Number of subjects included in analysis | 127 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[5] |
| P-value | < 0.0001 |
| Method | Regression, Logistic |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 20.86 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 4.18 |
| upper limit | 379.18 |

Notes:

[5] - Cohort A

Secondary: Radiological Progression Free Survival (rPFS) by blinded independent central review (BICR) - Cohort A+B

| | |
|------------------------|--|
| End point title | Radiological Progression Free Survival (rPFS) by blinded independent central review (BICR) - Cohort A+B |
| End point description: | The time from randomisation until the date of objective radiological disease progression (by RECIST 1.1 and Prostate Cancer Working Group 3 (PCWG-3)) or death (by any cause in the absence of progression) regardless of whether the patient withdrew from randomised therapy or received another anti-cancer therapy prior to progression. |
| End point type | Secondary |
| End point timeframe: | Tumor assessments every 8 weeks from randomisation until radiographic progression assessed by BICR (median duration of treatment of 7 and 4 months for Olaparib and Investigators Choice of NHA respectively). |

| End point values | Cohort A+B Olaparib 300mg bd | Cohort A+B Investigators Choice of NHA | | |
|----------------------------------|------------------------------------|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 256 | 131 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 5.82 (5.52 to 7.36) | 3.52 (2.2 to 3.65) | | |

Statistical analyses

| Statistical analysis title | Secondary analysis |
|---|---|
| Comparison groups | Cohort A+B Investigators Choice of NHA v Cohort A+B Olaparib 300mg bd |
| Number of subjects included in analysis | 387 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[6] |
| P-value | < 0.0001 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.49 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.38 |
| upper limit | 0.63 |

Notes:

[6] - Cohort A+B

Secondary: Time to pain progression - Cohort A only

| | |
|------------------------|---|
| End point title | Time to pain progression - Cohort A only ^[7] |
| End point description: | Time from randomisation to time point at which worsening in pain is observed (ie date of pain progression - date of randomisation + 1). Based on average Brief Pain Inventory - short form (BPI-SF) worst pain [Item 3] and Analgesic Quantification Algorithm [AQA] score. |
| End point type | Secondary |

End point timeframe:

Every 4 weeks from randomisation (for 7 consecutive days) throughout the study (median duration of treatment of 7 and 4 months for Olaparib and Investigators Choice of NHA respectively).

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The study was designed to formally test these endpoints in only Cohort A patients, there is just 1 endpoint that is formally tested for both Cohort A and Cohort B which is rPFS. All other analyses are descriptive only

| End point values | Cohort A Olaparib 300mg bd | Cohort A Investigators choice of NHA | | |
|----------------------------------|---|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 162 | 83 | | |
| Units: Months | | | | |
| median (confidence interval 95%) | 99999999 (- 99999999 to 99999999) | 9.92 (5.39 to 99999999) | | |

Statistical analyses

| Statistical analysis title | Secondary analysis |
|---|---|
| Comparison groups | Cohort A Olaparib 300mg bd v Cohort A Investigators choice of NHA |
| Number of subjects included in analysis | 245 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[8] |
| P-value | = 0.0192 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.44 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.22 |
| upper limit | 0.91 |

Notes:

[8] - Cohort A

Secondary: Overall Survival (OS) - Cohort A only

| | |
|--|--|
| End point title | Overall Survival (OS) - Cohort A only ^[9] |
| End point description: | |
| Number of Participants with Overall Survival (OS) - Cohort A only. | |
| End point type | Secondary |

End point timeframe:

Approximately 35 months after the first patient was randomised.

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The study was designed to formally test these endpoints in only Cohort A patients, there is just 1 endpoint that is formally tested for both Cohort A and Cohort B which is rPFS. All other analyses are descriptive only

| End point values | Cohort A Olaparib 300mg bd | Cohort A Investigators choice of NHA | | |
|-----------------------------|----------------------------------|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 162 | 83 | | |
| Units: Participants | | | | |
| Died | 91 | 57 | | |
| Alive at data cut-off | 49 | 21 | | |

| | | | | |
|---|----|---|--|--|
| Terminated prior to death (withdrawn consent) | 22 | 5 | | |
|---|----|---|--|--|

Statistical analyses

| | |
|---|---|
| Statistical analysis title | Secondary analysis |
| Comparison groups | Cohort A Olaparib 300mg bd v Cohort A Investigators choice of NHA |
| Number of subjects included in analysis | 245 |
| Analysis specification | Pre-specified |
| Analysis type | superiority ^[10] |
| P-value | = 0.0175 |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.69 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.5 |
| upper limit | 0.97 |

Notes:

[10] - Cohort A

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the time of signature of informed consent throughout the treatment period (median duration of treatment of 7.5 and 3.9 months for Olaparib and Investigators Choice of NHA respectively) up to and including the 30-day follow-up period

Adverse event reporting additional description:

131 subjects randomised to Investigators Choice of NHA (IC) group (Full Analysis Set), however 1 subject did not receive treatment (resulting in 130 in Safety Analysis Set). Hence for IC group, Total number at risk for all-cause mortality = 131, Total # at Risk by any Serious Adverse Event = 130 and Total # at Risk by any Other Adverse Event = 130

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

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 22.1 |

Reporting groups

| | |
|-----------------------|--|
| Reporting group title | Cohort A+B Investigators choice of NHA |
|-----------------------|--|

Reporting group description:

either enzalutamide capsules (160 mg od) or abiraterone acetate tablets (1,000 mg od with 5 mg bid prednisone)

| | |
|-----------------------|------------------------------|
| Reporting group title | Cohort A+B Olaparib 300mg bd |
|-----------------------|------------------------------|

Reporting group description:

2x150mg film-coated tablets

| Serious adverse events | Cohort A+B Investigators choice of NHA | Cohort A+B Olaparib 300mg bd | |
|---|--|---------------------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 39 / 130 (30.00%) | 94 / 256 (36.72%) | |
| number of deaths (all causes) | 88 | 160 | |
| number of deaths resulting from adverse events | 1 | 1 | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Transitional cell carcinoma | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 130 (0.77%) | 0 / 256 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Glioma | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 130 (0.00%) | 1 / 256 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------------------------|-----------------------------------|--|
| Gastric cancer alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 130 (0.77%) 0 / 1 0 / 0 | 0 / 256 (0.00%) 0 / 0 0 / 0 | |
| Vascular disorders Deep vein thrombosis alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 130 (0.77%) 0 / 1 0 / 0 | 0 / 256 (0.00%) 0 / 0 0 / 0 | |
| Embolism alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 130 (0.00%) 0 / 0 0 / 0 | 1 / 256 (0.39%) 1 / 1 0 / 0 | |
| Orthostatic hypotension alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 130 (0.00%) 0 / 0 0 / 0 | 1 / 256 (0.39%) 0 / 1 0 / 0 | |
| Arterial thrombosis alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 130 (0.77%) 0 / 1 0 / 1 | 0 / 256 (0.00%) 0 / 0 0 / 0 | |
| Phlebitis alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 130 (0.00%) 0 / 0 0 / 0 | 1 / 256 (0.39%) 0 / 1 0 / 0 | |
| General disorders and administration site conditions Asthenia | | | |

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|--|-----------------|-----------------|--|
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 130 (0.77%) | 4 / 256 (1.56%) | |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Death | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 130 (0.77%) | 0 / 256 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | |
| Fatigue | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 130 (0.00%) | 2 / 256 (0.78%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sudden death | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 130 (0.00%) | 1 / 256 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Pyrexia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 130 (1.54%) | 3 / 256 (1.17%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pain | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 130 (0.00%) | 1 / 256 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General physical health deterioration | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

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|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 130 (0.77%) | 0 / 256 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pneumonia aspiration | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 130 (0.00%) | 3 / 256 (1.17%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pleural effusion | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 130 (0.77%) | 0 / 256 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | |
| Interstitial lung disease | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 130 (0.00%) | 1 / 256 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dyspnoea | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 130 (0.77%) | 4 / 256 (1.56%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chronic obstructive pulmonary disease | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 130 (0.00%) | 1 / 256 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonitis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

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|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 130 (0.00%) | 1 / 256 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumothorax | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 130 (0.00%) | 2 / 256 (0.78%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory failure | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 130 (0.00%) | 1 / 256 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pulmonary embolism | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 130 (0.77%) | 5 / 256 (1.95%) | |
| occurrences causally related to treatment / all | 0 / 1 | 2 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Delirium | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 130 (0.77%) | 1 / 256 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Confusional state | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 130 (0.00%) | 1 / 256 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Ankle fracture | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

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|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 130 (0.00%) | 1 / 256 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Concussion | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 130 (0.00%) | 1 / 256 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cystitis radiation | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 130 (0.00%) | 1 / 256 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fall | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 130 (1.54%) | 1 / 256 (0.39%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Femur fracture | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 130 (0.00%) | 3 / 256 (1.17%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Fracture | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 130 (0.00%) | 1 / 256 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis radiation | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 130 (0.00%) | 1 / 256 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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| Post-traumatic pain alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 130 (0.00%) 0 / 0 0 / 0 | 1 / 256 (0.39%) 0 / 1 0 / 0 | |
| Spinal compression fracture alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 130 (0.00%) 0 / 0 0 / 0 | 1 / 256 (0.39%) 0 / 1 0 / 0 | |
| Spinal fracture alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 130 (0.00%) 0 / 0 0 / 0 | 1 / 256 (0.39%) 0 / 1 0 / 0 | |
| Subdural haematoma alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 130 (0.77%) 0 / 1 0 / 0 | 0 / 256 (0.00%) 0 / 0 0 / 0 | |
| Cardiac disorders Acute coronary syndrome alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 130 (0.00%) 0 / 0 0 / 0 | 1 / 256 (0.39%) 1 / 1 0 / 0 | |
| Coronary ostial stenosis alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 130 (0.00%) 0 / 0 0 / 0 | 1 / 256 (0.39%) 0 / 1 0 / 0 | |
| Myocardial infarction alternative dictionary used: MedDRA 22.0 | | | |

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|--|-----------------|-----------------|--|--|
| subjects affected / exposed | 1 / 130 (0.77%) | 1 / 256 (0.39%) | | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | | |
| Right ventricular failure alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 0 / 130 (0.00%) | 1 / 256 (0.39%) | | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| Cardiopulmonary failure alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 0 / 130 (0.00%) | 2 / 256 (0.78%) | | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 2 | | |
| Cardiomyopathy alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 1 / 130 (0.77%) | 0 / 256 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |
| Cardiac failure acute alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 0 / 130 (0.00%) | 1 / 256 (0.39%) | | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | | |
| Cardiac failure alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 1 / 130 (0.77%) | 0 / 256 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | | |
| Atrial fibrillation alternative dictionary used: MedDRA 22.0 | | | | |
| subjects affected / exposed | 0 / 130 (0.00%) | 1 / 256 (0.39%) | | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | | |

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| Angina pectoris alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 2 / 130 (1.54%) 0 / 2 0 / 0 | 1 / 256 (0.39%) 1 / 1 0 / 0 | |
| Coronary artery stenosis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 130 (0.77%) 0 / 1 0 / 0 | 0 / 256 (0.00%) 0 / 0 0 / 0 | |
| Nervous system disorders Cerebrovascular accident alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 130 (0.00%) 0 / 0 0 / 0 | 3 / 256 (1.17%) 1 / 3 0 / 0 | |
| Cerebral infarction alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 130 (0.00%) 0 / 0 0 / 0 | 1 / 256 (0.39%) 0 / 1 0 / 0 | |
| Ballismus alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 130 (0.77%) 0 / 1 0 / 0 | 0 / 256 (0.00%) 0 / 0 0 / 0 | |
| Neuralgia alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 130 (0.00%) 0 / 0 0 / 0 | 1 / 256 (0.39%) 0 / 1 0 / 0 | |
| Ischaemic stroke alternative dictionary used: MedDRA 22.0 | | | |

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|---|-----------------|------------------|--|
| subjects affected / exposed | 1 / 130 (0.77%) | 0 / 256 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dizziness | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 130 (0.00%) | 1 / 256 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal cord compression | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 130 (0.77%) | 1 / 256 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Syncope | | | |
| subjects affected / exposed | 0 / 130 (0.00%) | 1 / 256 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Pancytopenia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 130 (0.00%) | 1 / 256 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thrombocytopenia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 130 (0.00%) | 4 / 256 (1.56%) | |
| occurrences causally related to treatment / all | 0 / 0 | 3 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anaemia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 130 (0.00%) | 23 / 256 (8.98%) | |
| occurrences causally related to treatment / all | 0 / 0 | 18 / 24 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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| Febrile neutropenia alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 130 (0.77%) 0 / 1 0 / 0 | 1 / 256 (0.39%) 1 / 1 0 / 0 | |
| Neutropenia alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 130 (0.00%) 0 / 0 0 / 0 | 3 / 256 (1.17%) 3 / 3 1 / 1 | |
| Eye disorders Diplopia alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 130 (0.00%) 0 / 0 0 / 0 | 1 / 256 (0.39%) 0 / 1 0 / 0 | |
| Gastrointestinal disorders Abdominal pain alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 130 (0.00%) 0 / 0 0 / 0 | 1 / 256 (0.39%) 0 / 1 0 / 0 | |
| Obstructive pancreatitis alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 130 (0.00%) 0 / 0 0 / 0 | 1 / 256 (0.39%) 0 / 1 0 / 0 | |
| Obstruction gastric alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 130 (0.00%) 0 / 0 0 / 0 | 1 / 256 (0.39%) 0 / 1 0 / 0 | |
| Nausea alternative dictionary used: MedDRA 22.0 | | | |

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| subjects affected / exposed | 2 / 130 (1.54%) | 2 / 256 (0.78%) | |
| occurrences causally related to treatment / all | 1 / 2 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Inguinal hernia alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 130 (0.77%) | 0 / 256 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastric ulcer haemorrhage alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 130 (0.77%) | 0 / 256 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastric ulcer alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 130 (0.00%) | 1 / 256 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diverticulum intestinal alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 130 (0.00%) | 1 / 256 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Diarrhoea alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 130 (0.00%) | 1 / 256 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Small intestinal obstruction alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 130 (0.77%) | 0 / 256 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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|---|-----------------------------------|-----------------------------------|--|
| Vomiting alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 130 (0.77%) 0 / 1 0 / 0 | 4 / 256 (1.56%) 3 / 4 0 / 0 | |
| Stress ulcer alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 130 (0.00%) 0 / 0 0 / 0 | 1 / 256 (0.39%) 0 / 1 0 / 0 | |
| Duodenal ulcer perforation subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 130 (0.77%) 0 / 1 0 / 1 | 0 / 256 (0.00%) 0 / 0 0 / 0 | |
| Hepatobiliary disorders Cholecystitis acute alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 130 (0.00%) 0 / 0 0 / 0 | 1 / 256 (0.39%) 0 / 1 0 / 0 | |
| Cholangitis alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 130 (0.00%) 0 / 0 0 / 0 | 1 / 256 (0.39%) 0 / 1 0 / 0 | |
| Budd-Chiari syndrome alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 130 (0.00%) 0 / 0 0 / 0 | 1 / 256 (0.39%) 0 / 1 0 / 1 | |
| Skin and subcutaneous tissue disorders Drug eruption alternative dictionary used: MedDRA 22.0 | | | |

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|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 130 (0.77%) | 0 / 256 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin ulcer | | | |
| subjects affected / exposed | 0 / 130 (0.00%) | 1 / 256 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 130 (1.54%) | 1 / 256 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 2 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chronic kidney disease | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 130 (0.77%) | 0 / 256 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Calculus bladder | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 130 (0.00%) | 1 / 256 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hydronephrosis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 130 (0.77%) | 1 / 256 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Haematuria | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 130 (0.77%) | 3 / 256 (1.17%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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| Nephrolithiasis alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 130 (0.77%) 0 / 1 0 / 0 | 0 / 256 (0.00%) 0 / 0 0 / 0 | |
| Urinary tract obstruction alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 2 / 130 (1.54%) 0 / 2 0 / 0 | 0 / 256 (0.00%) 0 / 0 0 / 0 | |
| Urinary retention alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 130 (0.00%) 0 / 0 0 / 0 | 2 / 256 (0.78%) 0 / 2 0 / 1 | |
| Renal impairment alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 130 (0.00%) 0 / 0 0 / 0 | 1 / 256 (0.39%) 1 / 1 0 / 0 | |
| Renal failure alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 130 (0.00%) 0 / 0 0 / 0 | 1 / 256 (0.39%) 0 / 1 0 / 0 | |
| Endocrine disorders Adrenal insufficiency alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 0 / 130 (0.00%) 0 / 0 0 / 0 | 1 / 256 (0.39%) 0 / 1 0 / 0 | |
| Musculoskeletal and connective tissue disorders Back pain | | | |

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|--|-----------------|-----------------|--|
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 130 (0.77%) | 1 / 256 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Arthralgia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 130 (0.00%) | 1 / 256 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal pain | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 130 (0.00%) | 1 / 256 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal chest pain | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 130 (0.00%) | 2 / 256 (0.78%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Muscular weakness | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 130 (0.00%) | 2 / 256 (0.78%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bone pain | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 130 (0.00%) | 2 / 256 (0.78%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Spinal stenosis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 130 (0.00%) | 1 / 256 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Infections and infestations | | | |
| Cystitis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 130 (0.77%) | 0 / 256 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cellulitis of male external genital organ | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 130 (0.00%) | 1 / 256 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Anal abscess | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 130 (0.77%) | 0 / 256 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 130 (0.77%) | 0 / 256 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urosepsis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 130 (0.77%) | 0 / 256 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|---|-----------------|------------------|--|
| subjects affected / exposed | 4 / 130 (3.08%) | 5 / 256 (1.95%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sepsis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 3 / 130 (2.31%) | 3 / 256 (1.17%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyelonephritis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 130 (0.00%) | 1 / 256 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 4 / 130 (3.08%) | 11 / 256 (4.30%) | |
| occurrences causally related to treatment / all | 0 / 4 | 2 / 13 | |
| deaths causally related to treatment / all | 0 / 3 | 1 / 3 | |
| Pharyngitis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 130 (0.00%) | 1 / 256 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infection | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 1 / 130 (0.77%) | 0 / 256 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Septic shock | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 130 (0.00%) | 1 / 256 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |

| | | | |
|---|-----------------|-----------------|--|
| Pneumocystis jirovecii pneumoni | | | |
| subjects affected / exposed | 0 / 130 (0.00%) | 1 / 256 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nasopharyngitis | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 130 (0.00%) | 1 / 256 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 130 (0.00%) | 2 / 256 (0.78%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dehydration | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 3 / 130 (2.31%) | 0 / 256 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypocalcaemia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 130 (0.00%) | 1 / 256 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypoglycaemia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 0 / 130 (0.00%) | 1 / 256 (0.39%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyponatraemia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 130 (0.00%) | 2 / 256 (0.78%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Cohort A+B Investigators choice of NHA | Cohort A+B Olaparib 300mg bd | |
|---|--|---------------------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 112 / 130 (86.15%) | 241 / 256 (94.14%) | |
| Investigations | | | |
| Weight decreased | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 7 / 130 (5.38%) | 21 / 256 (8.20%) | |
| occurrences (all) | 7 | 21 | |
| Nervous system disorders | | | |
| Headache | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 3 / 130 (2.31%) | 16 / 256 (6.25%) | |
| occurrences (all) | 3 | 29 | |
| Dysgeusia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 2 / 130 (1.54%) | 18 / 256 (7.03%) | |
| occurrences (all) | 2 | 20 | |
| Dizziness | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 5 / 130 (3.85%) | 17 / 256 (6.64%) | |
| occurrences (all) | 5 | 18 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |
| subjects affected / exposed | 20 / 130 (15.38%) | 110 / 256 (42.97%) | |
| occurrences (all) | 23 | 154 | |
| Neutropenia | | | |
| alternative dictionary used: MedDRA 22.0 | | | |

| | | | |
|--|---|--|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Lymphopenia</p> <p>alternative dictionary used: MedDRA 22.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Thrombocytopenia</p> <p>alternative dictionary used: MedDRA 22.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>0 / 130 (0.00%)</p> <p>0</p> <p>1 / 130 (0.77%)</p> <p>1</p> <p>2 / 130 (1.54%)</p> <p>2</p> | <p>13 / 256 (5.08%)</p> <p>16</p> <p>13 / 256 (5.08%)</p> <p>15</p> <p>18 / 256 (7.03%)</p> <p>22</p> | |
| <p>General disorders and administration site conditions</p> <p>Oedema peripheral</p> <p>alternative dictionary used: MedDRA 22.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pyrexia</p> <p>alternative dictionary used: MedDRA 22.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Fatigue</p> <p>alternative dictionary used: MedDRA 22.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Asthenia</p> <p>alternative dictionary used: MedDRA 22.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>10 / 130 (7.69%)</p> <p>10</p> <p>4 / 130 (3.08%)</p> <p>4</p> <p>28 / 130 (21.54%)</p> <p>28</p> <p>18 / 130 (13.85%)</p> <p>19</p> | <p>34 / 256 (13.28%)</p> <p>36</p> <p>15 / 256 (5.86%)</p> <p>16</p> <p>68 / 256 (26.56%)</p> <p>71</p> <p>37 / 256 (14.45%)</p> <p>54</p> | |
| <p>Gastrointestinal disorders</p> <p>Constipation</p> <p>alternative dictionary used: MedDRA 22.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Dyspepsia</p> <p>alternative dictionary used: MedDRA 22.0</p> | <p>19 / 130 (14.62%)</p> <p>21</p> | <p>49 / 256 (19.14%)</p> <p>52</p> | |

| | | | |
|--|---|--|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Diarrhoea</p> <p>alternative dictionary used: MedDRA 22.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Vomiting</p> <p>alternative dictionary used: MedDRA 22.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Nausea</p> <p>alternative dictionary used: MedDRA 22.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Stomatitis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>3 / 130 (2.31%)</p> <p>3</p> <p>9 / 130 (6.92%)</p> <p>9</p> <p>17 / 130 (13.08%)</p> <p>19</p> <p>26 / 130 (20.00%)</p> <p>28</p> <p>2 / 130 (1.54%)</p> <p>2</p> | <p>20 / 256 (7.81%)</p> <p>23</p> <p>54 / 256 (21.09%)</p> <p>71</p> <p>49 / 256 (19.14%)</p> <p>82</p> <p>109 / 256 (42.58%)</p> <p>136</p> <p>13 / 256 (5.08%)</p> <p>14</p> | |
| <p>Respiratory, thoracic and mediastinal disorders</p> <p>Cough</p> <p>alternative dictionary used: MedDRA 22.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Dyspnoea</p> <p>alternative dictionary used: MedDRA 22.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>3 / 130 (2.31%)</p> <p>3</p> <p>4 / 130 (3.08%)</p> <p>4</p> | <p>29 / 256 (11.33%)</p> <p>32</p> <p>24 / 256 (9.38%)</p> <p>25</p> | |
| <p>Psychiatric disorders</p> <p>Insomnia</p> <p>alternative dictionary used: MedDRA 22.0</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>4 / 130 (3.08%)</p> <p>4</p> | <p>14 / 256 (5.47%)</p> <p>14</p> | |
| <p>Renal and urinary disorders</p> <p>Haematuria</p> <p>alternative dictionary used: MedDRA 22.0</p> | | | |

| | | | |
|---|-------------------------|-------------------------|--|
| subjects affected / exposed occurrences (all) | 10 / 130 (7.69%) 11 | 6 / 256 (2.34%) 7 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 14 / 130 (10.77%) 16 | 25 / 256 (9.77%) 26 | |
| Back pain alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 17 / 130 (13.08%) 18 | 36 / 256 (14.06%) 44 | |
| Musculoskeletal pain alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 6 / 130 (4.62%) 6 | 17 / 256 (6.64%) 18 | |
| Musculoskeletal chest pain alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 6 / 130 (4.62%) 7 | 14 / 256 (5.47%) 14 | |
| Pain in extremity subjects affected / exposed occurrences (all) | 6 / 130 (4.62%) 6 | 14 / 256 (5.47%) 18 | |
| Infections and infestations | | | |
| Urinary tract infection alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 12 / 130 (9.23%) 15 | 18 / 256 (7.03%) 22 | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite alternative dictionary used: MedDRA 22.0 subjects affected / exposed occurrences (all) | 24 / 130 (18.46%) 25 | 78 / 256 (30.47%) 88 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---------------|---|
| 09 March 2017 | Version 2.0: Administration of other anti-cancer agents: remove following text "corticosteroids for the symptomatic control of brain metastases" because subjects with known brain metastases are excluded from the study |
| 04 June 2018 | Version 3.0: Abiraterone acetate 500mg tablets added to treatment regimens |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported