



## Clinical trial results:

### A Phase II, Open-label Study to Assess the Efficacy, Safety, and Tolerability of AZD4635 in Combination with Durvalumab and in Combination with Cabazitaxel and Durvalumab in Patients Who Have Progressive Metastatic Castrate-Resistant Prostate Cancer (AARDVARC) Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2020-000209-10 |
| Trial protocol           | BE DE FR DK NL |
| Global end of trial date | 08 August 2022 |

#### Results information

|                                |                |
|--------------------------------|----------------|
| Result version number          | v1 (current)   |
| This version publication date  | 23 August 2023 |
| First version publication date | 23 August 2023 |

#### Trial information

##### Trial identification

|                       |             |
|-----------------------|-------------|
| Sponsor protocol code | D8731C00002 |
|-----------------------|-------------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT04495179 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | AstraZeneca   |
| Sponsor organisation address | NA, NA, United States, NA   |
| Public contact               | Global Clinical Head, AstraZeneca Clinical Study Information Center, +1 87724094 79, <a href="mailto:information.center@astrazeneca.com">information.center@astrazeneca.com</a> |
| Scientific contact           | Global Clinical Head, AstraZeneca Clinical Study Information Center, +1 87724094 79, <a href="mailto:information.center@astrazeneca.com">information.center@astrazeneca.com</a> |

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                       | 29 April 2022  |
| Is this the analysis of the primary completion data? | No             |
| Global end of trial reached?                         | Yes            |
| Global end of trial date                             | 08 August 2022 |
| Was the trial ended prematurely?                     | No             |

Notes:

## General information about the trial

Main objective of the trial:

To determine the efficacy (as assessed by radiographic progression free survival [rPFS]) of AZD4635 plus durvalumab and separately of AZD4635 plus durvalumab plus cabazitaxel in participants with metastatic castrate-resistant prostate cancer (mCRPC).

Protection of trial subjects:

This study was conducted in accordance with the protocol and with the consensus ethical principles derived from international guidelines including the Declaration of Helsinki and Council for International Organisations of Medical Sciences (CIOMS) International Ethical Guidelines, applicable International Council for Harmonisation Good Clinical Practice (ICH GCP) Guidelines, and the applicable laws and regulations

Background therapy: -

Evidence for comparator: -

|   |                |
|---|----------------|
| Actual start date of recruitment                          | 04 August 2020 |
| Long term follow-up planned                               | No             |
| Independent data monitoring committee (IDMC) involvement? | No             |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |                       |
|--------------------------------------|-----------------------|
| Country: Number of subjects enrolled | Belgium: 4            |
| Country: Number of subjects enrolled | France: 3             |
| Country: Number of subjects enrolled | Korea, Republic of: 4 |
| Country: Number of subjects enrolled | Spain: 8              |
| Country: Number of subjects enrolled | United States: 11     |
| Worldwide total number of subjects   | 30                    |
| EEA total number of subjects         | 15                    |

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)      | 8  |
| From 65 to 84 years       | 22 |
| 85 years and over         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

Participants were enrolled in this study from 04-August-2020 to 08-August-2022.

### Pre-assignment

Screening details:

Participants who met the inclusion and none of the exclusion criteria were enrolled to the study. All study assessments were performed as per the schedule of assessment.

### Period 1

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

### Arms

|                              |                             |
|------------------------------|-----------------------------|
| Are arms mutually exclusive? | Yes                         |
| <b>Arm title</b>             | Arm A: AZD4635 + durvalumab |

Arm description:

Participants received AZD4635 Dose A orally daily, and durvalumab Dose B intravenously every 4 weeks.

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | AZD4635      |
| Investigational medicinal product code |              |
| Other name                             |              |
| Pharmaceutical forms                   | Capsule      |
| Routes of administration               | Oral use     |

Dosage and administration details:

Participants were administered AZD4635 75 mg tablets orally daily.

|  |   |
|--|---|
| Investigational medicinal product name | Durvalumab                                      |
| Investigational medicinal product code |   |
| Other name                             |   |
| Pharmaceutical forms                   | Capsule, Concentrate for solution for injection |
| Routes of administration               | Oral use, Intravenous use                       |

Dosage and administration details:

Participants were administered durvalumab 1500 mg intravenously (IV) every 4 weeks (Q4W).

|                  |   |
|------------------|---|
| <b>Arm title</b> | Arm B: AZD4635 + durvalumab + cabazitaxel |
|------------------|---|

Arm description:

Participants received AZD4635 Dose A orally daily, durvalumab Dose B intravenously (IV) every 3 weeks (Q3W), and cabazitaxel Dose C IV Q3W

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | AZD4635      |
| Investigational medicinal product code |              |
| Other name                             |              |
| Pharmaceutical forms                   | Capsule      |
| Routes of administration               | Oral use     |

Dosage and administration details:

Participants were administered AZD4635 75 mg tablets orally daily.

|  |   |
|--|---|
| Investigational medicinal product name   | Cabazitaxel                                     |
| Investigational medicinal product code   |   |
| Other name   |   |
| Pharmaceutical forms   | Capsule, Concentrate for solution for injection |
| Routes of administration   | Oral use, Intravenous use                       |
| Dosage and administration details:   |   |
| Participants were administered cabazitaxel 20 or 25 mg/m <sup>2</sup> intravenously every 3 weeks (Q3W). |   |
| Investigational medicinal product name   | Durvalumab                                      |
| Investigational medicinal product code   |   |
| Other name   |   |
| Pharmaceutical forms   | Concentrate for solution for injection          |
| Routes of administration   | Intravenous use                                 |

Dosage and administration details:

Participants were administered durvalumab 1500 mg intravenously every 4 weeks.

| Number of subjects in period 1 | Arm A: AZD4635 +<br>durvalumab | Arm B: AZD4635 +<br>durvalumab +<br>cabazitaxel |
|--------------------------------|--------------------------------|---|
|                                |                                |   |
| Started                        | 2                              | 28  |
| Completed                      | 0                              | 0   |
| Not completed                  | 2                              | 28  |
| Adverse event, serious fatal   | -                              | 4   |
| Consent withdrawn by subject   | 2                              | 4   |
| Adverse event, non-fatal       | -                              | 1   |
| Study terminated by sponsor    | -                              | 18  |
| Lost to follow-up              | -                              | 1   |

## Baseline characteristics

### Reporting groups

|  |   |
|--|---|
| Reporting group title  | Arm A: AZD4635 + durvalumab               |
| Reporting group description:   |   |
| Participants received AZD4635 Dose A orally daily, and durvalumab Dose B intravenously every 4 weeks.                                      |   |
| Reporting group title  | Arm B: AZD4635 + durvalumab + cabazitaxel |
| Reporting group description:   |   |
| Participants received AZD4635 Dose A orally daily, durvalumab Dose B intravenously (IV) every 3 weeks (Q3W), and cabazitaxel Dose C IV Q3W |   |

| Reporting group values   | Arm A: AZD4635 + durvalumab | Arm B: AZD4635 + durvalumab + cabazitaxel | Total |
|--|-----------------------------|---|-------|
| Number of subjects   | 2                           | 28  | 30    |
| 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)   | 1                           | 7   | 8     |
| From 65-84 years   | 1                           | 21  | 22    |
| 85 years and over  | 0                           | 0   | 0     |
| Age Continuous   |                             |   |       |
| Units: years   |                             |   |       |
| arithmetic mean  | 0                           | 68.0                                      |       |
| standard deviation   | ± 0                         | ± 8.18                                    | -     |
| Sex/Gender, Customized   |                             |   |       |
| Units: Participants  |                             |   |       |
| Male   | 2                           | 28  | 30    |
| Race (NIH/OMB)   |                             |   |       |
| Units: Subjects  |                             |   |       |
| American Indian or Alaska Native   | 0                           | 0   | 0     |
| Asian  | 0                           | 5   | 5     |
| Native Hawaiian or Other Pacific Islander  | 0                           | 0   | 0     |
| Black or African American  | 0                           | 0   | 0     |
| White  | 0                           | 19  | 19    |
| More than one race   | 0                           | 0   | 0     |
| Unknown or Not Reported  | 2                           | 4   | 6     |
| Ethnicity (NIH/OMB)  |                             |   |       |
| The data for Arm A was not calculated because of only two participants in this arm due to which there will be a patient identification risk. |                             |   |       |
| Units: Subjects  |                             |   |       |
| Hispanic or Latino   | 0                           | 4   | 4     |
| Not Hispanic or Latino   | 0                           | 21  | 21    |

|                         |   |   |   |
|-------------------------|---|---|---|
| Unknown or Not Reported | 2 | 3 | 5 |
|-------------------------|---|---|---|

## End points

### End points reporting groups

|  |   |
|--|---|
| Reporting group title  | Arm A: AZD4635 + durvalumab               |
| Reporting group description:<br>Participants received AZD4635 Dose A orally daily, and durvalumab Dose B intravenously every 4 weeks.                                      |   |
| Reporting group title  | Arm B: AZD4635 + durvalumab + cabazitaxel |
| Reporting group description:<br>Participants received AZD4635 Dose A orally daily, durvalumab Dose B intravenously (IV) every 3 weeks (Q3W), and cabazitaxel Dose C IV Q3W |   |

### Primary: Radiographic Progression Free Survival (rPFS) in each arm separately to determine the efficacy of AZD4635 plus durvalumab and of AZD4635 plus durvalumab plus cabazitaxel in patients with metastatic castrate-resistant prostate cancer (mCRPC)

|  |   |
|--|---|
| End point title  | Radiographic Progression Free Survival (rPFS) in each arm separately to determine the efficacy of AZD4635 plus durvalumab and of AZD4635 plus durvalumab plus cabazitaxel in patients with metastatic castrate-resistant prostate cancer (mCRPC) <sup>[1]</sup> |
| End point description:<br>rPFS was defined as the time from first dose to radiographic progression, assessed by the Investigator per RECIST 1.1 (soft tissue) and PCWG3 (Prostate Cancer Working Group 3) criteria [bone] or death from any cause, whichever occurred first. |   |
| End point type   | Primary   |
| End point timeframe:<br>From first dose to first documented progression or death from any cause (whichever comes first) (approximately 1 year)   |   |

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: Statistical Analyses were not performed for these Outcome Measures as this study is non-comparative.

| End point values                 | Arm A:<br>AZD4635 +<br>durvalumab | Arm B:<br>AZD4635 +<br>durvalumab +<br>cabazitaxel |  |  |
|----------------------------------|-----------------------------------|--|--|--|
| Subject group type               | Reporting group                   | Reporting group                                    |  |  |
| Number of subjects analysed      | 0 <sup>[2]</sup>                  | 28 <sup>[3]</sup>                                  |  |  |
| Units: months                    |                                   |  |  |  |
| median (confidence interval 95%) | ( to )                            | 5.8 (4.2 to 9999.9999)                             |  |  |

Notes:

[2] - The data for Arm A was not calculated because of a patient identification risk.

[3] - "9999.9999" indicates that a upper limit was not calculated due to not enough events at later times.

### Statistical analyses

No statistical analyses for this end point

### Secondary: rPFS by adenosine (ADO) signalling gene expression in high and low



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**subgroups to determine the efficacy of AZD4635 plus durvalumab plus cabazitaxel in participants with mCRPC**

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|                 |   |
|-----------------|---|
| End point title | rPFS by adenosine (ADO) signalling gene expression in high and low subgroups to determine the efficacy of AZD4635 plus durvalumab plus cabazitaxel in participants with mCRPC |
|-----------------|---|

End point description:

rPFS was defined as the time from first dose to radiographic progression, assessed by the Investigator per RECIST 1.1 (soft tissue) and PCWG3 criteria (bone) or death from any cause, whichever occurred first.

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

End point timeframe:

From first dose to first documented progression or death from any cause (whichever comes first), up to two years

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| End point values            | Arm A:<br>AZD4635 +<br>durvalumab | Arm B:<br>AZD4635 +<br>durvalumab +<br>cabazitaxel |  |  |
|-----------------------------|-----------------------------------|--|--|--|
| Subject group type          | Reporting group                   | Reporting group                                    |  |  |
| Number of subjects analysed | 0 <sup>[4]</sup>                  | 27   |  |  |
| Units: Participants         |                                   |  |  |  |
| High ADO                    |                                   | 14   |  |  |
| Low ADO                     |                                   | 13   |  |  |

Notes:

[4] - The data for Arm A was not calculated because of a patient identification risk.

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**Statistical analyses**

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No statistical analyses for this end point

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**Secondary: Overall survival (OS) in each arm separately to determine the efficacy of AZD4635 plus durvalumab and of AZD4635 plus durvalumab plus cabazitaxel in participants with mCRPC**

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|                 |  |
|-----------------|--|
| End point title | Overall survival (OS) in each arm separately to determine the efficacy of AZD4635 plus durvalumab and of AZD4635 plus durvalumab plus cabazitaxel in participants with mCRPC |
|-----------------|--|

End point description:

OS was defined as the time from first dose until death due to any cause regardless of whether the participant withdrew from study treatment or received another anti-cancer therapy.

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

End point timeframe:

Arm A and B: Every 90 days from the last dose of study drug up to 2 years

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| End point values                 | Arm A:<br>AZD4635 +<br>durvalumab | Arm B:<br>AZD4635 +<br>durvalumab +<br>cabazitaxel |  |  |
|----------------------------------|-----------------------------------|--|--|--|
| Subject group type               | Reporting group                   | Reporting group                                    |  |  |
| Number of subjects analysed      | 0 <sup>[5]</sup>                  | 28 <sup>[6]</sup>                                  |  |  |
| Units: months                    |                                   |  |  |  |
| median (confidence interval 95%) | ( to )                            | 9999.9999 (7.9<br>to 9999.9999)                    |  |  |

Notes:

[5] - The data for Arm A was not calculated because of a patient identification risk.

[6] - "9999.9999" indicates that these values were not calculated as less than 50% patients died.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Subjects with Objective Response in Subjects with MCRPC who received AZD4635 Plus Durvalumab Plus Cabazitaxel

|                 |   |
|-----------------|---|
| End point title | Number of Subjects with Objective Response in Subjects with MCRPC who received AZD4635 Plus Durvalumab Plus Cabazitaxel |
|-----------------|---|

End point description:

Confirmed ORR was defined as the proportion of participants with a confirmed complete response (CR) or partial response (PR) using overall radiographic response assessed by RECIST v1.1 and PCWG-3 criteria (bone), and was based on a subset of all treated participants with measurable disease at baseline per the site Investigator.

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

End point timeframe:

From first dose to first documented progression or death from any cause (whichever comes first), up to two years

| End point values            | Arm A:<br>AZD4635 +<br>durvalumab | Arm B:<br>AZD4635 +<br>durvalumab +<br>cabazitaxel |  |  |
|-----------------------------|-----------------------------------|--|--|--|
| Subject group type          | Reporting group                   | Reporting group                                    |  |  |
| Number of subjects analysed | 0 <sup>[7]</sup>                  | 28   |  |  |
| Units: Participants         |                                   | 2  |  |  |

Notes:

[7] - The data for Arm A was not calculated because of a patient identification risk.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Subjects with Prostate-specificin Antigen (PSA50) Response in Subjects with MCRPC who Received AZD4635 Plus Durvalumab Plus Cabazitaxel

|                 |   |
|-----------------|---|
| End point title | Number of Subjects with Prostate-specificin Antigen (PSA50) Response in Subjects with MCRPC who Received AZD4635 Plus Durvalumab Plus Cabazitaxel |
|-----------------|---|

End point description:

Confirmed PSA50 response is defined as the proportion of participants who achieved a  $\geq 50\%$  decrease

in PSA from baseline to the lowest post-baseline PSA, confirmed by a consecutive PSA at least 3 weeks later and was based on PSA evaluable participants (dosed participants with an abnormal baseline PSA [ $\geq 1$  ng/mL]).

|   |           |
|---|-----------|
| End point type  | Secondary |
| End point timeframe:  |           |
| Arm A: Screening, Day 1 of each cycle up to 11 months (Each cycle was 28 days in length); Arm B: Screening, Day 1 of each cycle up to 11 months (Cycle 1 to Cycle 10 = 21 days, Cycle 11 onwards = 28 days) |           |

| End point values            | Arm A:<br>AZD4635 +<br>durvalumab | Arm B:<br>AZD4635 +<br>durvalumab +<br>cabazitaxel |  |  |
|-----------------------------|-----------------------------------|--|--|--|
| Subject group type          | Reporting group                   | Reporting group                                    |  |  |
| Number of subjects analysed | 0 <sup>[8]</sup>                  | 28   |  |  |
| Units: Participants         |                                   | 5  |  |  |

Notes:

[8] - The data for Arm A was not calculated because of a patient identification risk.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from baseline in worst pain in the daily activities scales of the Brief Pain Inventory – Short Form (BPI-SF)

|                 |   |
|-----------------|---|
| End point title | Change from baseline in worst pain in the daily activities scales of the Brief Pain Inventory – Short Form (BPI-SF) |
|-----------------|---|

End point description:

"Worst pain" and "Average pain" are 'single question' scores from the BPI short form and may take any value from 0 to 10 (worst outcome). "Interference Pain" is the total score of 7 sub-scores, where each value may take any value from 0 to 10 (worst outcome). The range of the "Interference Score" can be from 0 to 70.

Note: None of the 14 participants at Baseline answered the questionnaire at Cycle 1 Day 1. Therefore, related statistics were not derived for this timepoint.

n = Number of participants included in analysis

|  |           |
|--|-----------|
| End point type   | Secondary |
| End point timeframe:   |           |
| Arm A: Screening, Day 1 of each cycle up to 9 months (Each cycle was 28 days in length); Arm B: Screening, Day 1 of each cycle up to 9 months (Each cycle was 21 days in length) |           |

| End point values                     | Arm A:<br>AZD4635 +<br>durvalumab | Arm B:<br>AZD4635 +<br>durvalumab +<br>cabazitaxel |  |  |
|--------------------------------------|-----------------------------------|--|--|--|
| Subject group type                   | Reporting group                   | Reporting group                                    |  |  |
| Number of subjects analysed          | 0 <sup>[9]</sup>                  | 28 <sup>[10]</sup>                                 |  |  |
| Units: Score on a Scale              |                                   |  |  |  |
| arithmetic mean (standard deviation) |                                   |  |  |  |
| Baseline (n = 14)                    | ()                                | 3.4 ( $\pm$ 2.44)                                  |  |  |

|                        |    |                         |  |  |
|------------------------|----|-------------------------|--|--|
| Cycle 1 Day 1 (n = 0)  | () | 9999.9999 (± 9999.9999) |  |  |
| Cycle 2 Day 1 (n = 11) | () | -1.6 (± 2.94)           |  |  |
| Cycle 3 Day 1 (n = 13) | () | -0.3 (± 4.40)           |  |  |
| Cycle 4 Day 1 (n = 9)  | () | -1.6 (± 2.88)           |  |  |
| Cycle 5 Day 1 (n = 7)  | () | -2.1 (± 3.58)           |  |  |
| Cycle 6 Day 1 (n = 8)  | () | -1.9 (± 3.00)           |  |  |
| Cycle 7 Day 1 (n = 8)  | () | 1.0 (± 1.85)            |  |  |
| Cycle 8 Day 1 (n = 6)  | () | -1.7 (± 2.66)           |  |  |
| Cycle 9 Day 1 (n = 5)  | () | -0.2 (± 2.17)           |  |  |

Notes:

[9] - The data for Arm A was not calculated because of a patient identification risk.

[10] - Here, arbitrary value 9999.9999 indicates that the values are not available.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from baseline in average pain in the daily activities scales of the Brief Pain Inventory – Short Form (BPI-SF)

|                 |   |
|-----------------|---|
| End point title | Change from baseline in average pain in the daily activities scales of the Brief Pain Inventory – Short Form (BPI-SF) |
|-----------------|---|

End point description:

"Worst pain" and "Average pain" are 'single question' scores from the BPI short form and may take any value from 0 to 10 (worst outcome). "Interference Pain" is the total score of 7 sub-scores, where each value may take any value from 0 to 10 (worst outcome). The range of the "Interference Score" can be from 0 to 70.

Note: None of the 14 participants at Baseline answered the questionnaire at Cycle 1 Day 1. Therefore, related statistics were not derived for this timepoint.

n = Number of participants included in analysis

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

End point timeframe:

Arm A: Screening, Day 1 of each cycle up to 9 months (Each cycle was 28 days in length); Arm B: Screening, Day 1 of each cycle up to 9 months (Each cycle was 21 days in length)

| End point values                     | Arm A:<br>AZD4635 +<br>durvalumab | Arm B:<br>AZD4635 +<br>durvalumab +<br>cabazitaxel |  |  |
|--------------------------------------|-----------------------------------|--|--|--|
| Subject group type                   | Reporting group                   | Reporting group                                    |  |  |
| Number of subjects analysed          | 0 <sup>[11]</sup>                 | 28 <sup>[12]</sup>                                 |  |  |
| Units: Score on a Scale              |                                   |  |  |  |
| arithmetic mean (standard deviation) |                                   |  |  |  |
| Baseline (n = 14)                    | ()                                | 2.3 (± 2.09)                                       |  |  |
| Cycle 1 Day 1 (n = 0)                | ()                                | 9999.9999 (± 9999.9999)                            |  |  |
| Cycle 2 Day 1 (n = 11)               | ()                                | -1.3 (± 1.19)                                      |  |  |
| Cycle 3 Day 1 (n = 13)               | ()                                | 0.6 (± 3.15)                                       |  |  |
| Cycle 4 Day 1 (n = 9)                | ()                                | -0.9 (± 1.27)                                      |  |  |
| Cycle 5 Day 1 (n = 7)                | ()                                | -1.6 (± 2.15)                                      |  |  |
| Cycle 6 Day 1 (n = 8)                | ()                                | -1.4 (± 1.51)                                      |  |  |
| Cycle 7 Day 1 (n = 8)                | ()                                | 0.0 (± 1.41)                                       |  |  |

|                       |    |               |  |  |
|-----------------------|----|---------------|--|--|
| Cycle 8 Day 1 (n = 6) | () | -0.8 (± 1.47) |  |  |
| Cycle 9 Day 1 (n = 5) | () | -1.2 (± 0.84) |  |  |

Notes:

[11] - The data for Arm A was not calculated because of a patient identification risk.

[12] - Here, arbitrary value 9999.9999 indicates that the values are not available.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Change from baseline in pain interference in the daily activities scales of the Brief Pain Inventory – Short Form (BPI-SF)

|                 |  |
|-----------------|--|
| End point title | Change from baseline in pain interference in the daily activities scales of the Brief Pain Inventory – Short Form (BPI-SF) |
|-----------------|--|

End point description:

"Worst pain" and "Average pain" are 'single question' scores from the BPI short form and may take any value from 0 to 10 (worst outcome). "Interference Pain" is the total score of 7 sub-scores, where each value may take any value from 0 to 10 (worst outcome). The range of the "Interference Score" can be from 0 to 70.

Note: None of the 14 participants at Baseline answered the questionnaire at Cycle 1 Day 1. Therefore, related statistics were not derived for this timepoint.

n = Number of participants included in analysis

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

End point timeframe:

Arm A: Screening, Day 1 of each cycle up to 9 months (Each cycle was 28 days in length); Arm B: Screening, Day 1 of each cycle up to 9 months (Each cycle was 21 days in length)

| End point values                     | Arm A:<br>AZD4635 +<br>durvalumab | Arm B:<br>AZD4635 +<br>durvalumab +<br>cabazitaxel |  |  |
|--------------------------------------|-----------------------------------|--|--|--|
| Subject group type                   | Reporting group                   | Reporting group                                    |  |  |
| Number of subjects analysed          | 0 <sup>[13]</sup>                 | 28 <sup>[14]</sup>                                 |  |  |
| Units: Score on a Scale              |                                   |  |  |  |
| arithmetic mean (standard deviation) |                                   |  |  |  |
| Baseline (n = 14)                    | ()                                | 8.0 (± 8.47)                                       |  |  |
| Cycle 1 Day 1 (n = 0)                | ()                                | 9999.9999 (± 9999.9999)                            |  |  |
| Cycle 2 Day 1 (n = 11)               | ()                                | 2.5 (± 13.90)                                      |  |  |
| Cycle 3 Day 1 (n = 13)               | ()                                | 12.3 (± 18.96)                                     |  |  |
| Cycle 4 Day 1 (n = 9)                | ()                                | 4.9 (± 12.73)                                      |  |  |
| Cycle 5 Day 1 (n = 7)                | ()                                | 1.3 (± 5.19)                                       |  |  |
| Cycle 6 Day 1 (n = 8)                | ()                                | 2.0 (± 8.40)                                       |  |  |
| Cycle 7 Day 1 (n = 8)                | ()                                | 8.1 (± 9.93)                                       |  |  |
| Cycle 8 Day 1 (n = 6)                | ()                                | 7.2 (± 13.98)                                      |  |  |
| Cycle 9 Day 1 (n = 5)                | ()                                | 5.4 (± 15.16)                                      |  |  |

Notes:

[13] - The data for Arm A was not calculated because of a patient identification risk.

[14] - Here, arbitrary value 9999.9999 indicates that the values are not available.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Change from baseline in the FACT Advanced Prostate Symptom Index-6 (FAPSI-6), as derived from 6 items, the FAPSI-8 from 8 items within the FACT-P and the Prostate Cancer Symptoms (PCS), from the 12 items in the prostate-specific module of the FACT-P

|                 |   |
|-----------------|---|
| End point title | Change from baseline in the FACT Advanced Prostate Symptom Index-6 (FAPSI-6), as derived from 6 items, the FAPSI-8 from 8 items within the FACT-P and the Prostate Cancer Symptoms (PCS), from the 12 items in the prostate-specific module of the FACT-P |
|-----------------|---|

#### End point description:

The Functional Assessment of Cancer Therapy-Prostate (FACT-P) will be used to measure health related quality of life (HRQL) in men with prostate cancer. It consists of 4 subscales (physical, emotional, functional and social/family well-being) plus a 12-item prostate-specific module, the PCS subscale, which highlights concerns specific to participants with prostate cancer. Each question in the FACT-P questionnaires has a choice of 5 responses, "Not at all", "A little bit", "Somewhat", "Quite a bit" and "Very much". The scores range from 0 ("Not at all") to 4 ("Very much") for positively phrased questions. Negatively phrased questions have a reverse scoring, from 0 ("Very much") to 4 ("Not at all").

n = Number of participants included in analysis

Note: None of the 10 participants at Baseline answered the questionnaire at Cycle 1 Day 1. Therefore, related statistics were not derived for this timepoint.

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

#### End point timeframe:

Arm A: Screening, Day 1 of each cycle up to 9 months (Each cycle was 28 days in length); Arm B: Screening, Day 1 of each cycle up to 9 months (Each cycle was 21 days in length)

| End point values                     | Arm A:<br>AZD4635 +<br>durvalumab | Arm B:<br>AZD4635 +<br>durvalumab +<br>cabazitaxel |  |  |
|--------------------------------------|-----------------------------------|--|--|--|
| Subject group type                   | Reporting group                   | Reporting group                                    |  |  |
| Number of subjects analysed          | 0 <sup>[15]</sup>                 | 28 <sup>[16]</sup>                                 |  |  |
| Units: Score on a Scale              |                                   |  |  |  |
| arithmetic mean (standard deviation) |                                   |  |  |  |
| Baseline (n = 10)                    | ()                                | 16.6 (± 2.88)                                      |  |  |
| Cycle 1 Day 1 (n = 0)                | ()                                | 9999.9999 (± 9999.9999)                            |  |  |
| Cycle 2 Day 1 (n = 7)                | ()                                | 1.9 (± 1.68)                                       |  |  |
| Cycle 3 Day 1 (n = 9)                | ()                                | -0.7 (± 5.52)                                      |  |  |
| Cycle 4 Day 1 (n = 7)                | ()                                | -0.1 (± 3.34)                                      |  |  |
| Cycle 5 Day 1 (n = 5)                | ()                                | 0.6 (± 3.36)                                       |  |  |
| Cycle 6 Day 1 (n = 6)                | ()                                | 1.5 (± 1.38)                                       |  |  |
| Cycle 7 Day 1 (n = 7)                | ()                                | 0.0 (± 3.92)                                       |  |  |
| Cycle 8 Day 1 (n = 5)                | ()                                | -1.8 (± 4.15)                                      |  |  |
| Cycle 9 Day 1 (n = 4)                | ()                                | -3.0 (± 4.55)                                      |  |  |

Notes:

[15] - The data for Arm A was not calculated because of a patient identification risk.

[16] - Here, arbitrary value 9999.9999 indicates that the values are not available.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Subjects Who Progressed Based on BPI-SF Item 3

|   |  |
|---|--|
| End point title   | Number of Subjects Who Progressed Based on BPI-SF Item 3 |
| End point description:<br>Pain progression was assessed using BPI-SF.   |  |
| End point type  | Secondary  |
| End point timeframe:<br>Arm A: Screening, Day 1 of each cycle up to 12 months (Each cycle was 28 days in length); Arm B: Screening, Day 1 of each cycle up to 12 months (Cycle 1 to Cycle 10 = 21 days, Cycle 11 onwards = 28 days) |  |

| End point values            | Arm A:<br>AZD4635 +<br>durvalumab | Arm B:<br>AZD4635 +<br>durvalumab +<br>cabazitaxel |  |  |
|-----------------------------|-----------------------------------|--|--|--|
| Subject group type          | Reporting group                   | Reporting group                                    |  |  |
| Number of subjects analysed | 0 <sup>[17]</sup>                 | 28   |  |  |
| Units: Participants         |                                   | 1  |  |  |

Notes:

[17] - The data for Arm A was not calculated because of a patient identification risk.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Maximum observed plasma concentration (Cmax)

|   |  |
|---|--|
| End point title   | Maximum observed plasma concentration (Cmax) |
| End point description:<br>Investigate the PK of AZD4635 when given in combination with durvalumab, and when given in combination with durvalumab plus cabazitaxel.  |  |
| End point type  | Secondary                                    |
| End point timeframe:<br>Arm A: Cycle 1 to 3, and Cycle 4 onwards, and 90-day follow-up (FU) visit up to 14 months [Each cycle was 28 days in length]; Arm B: Cycle 1 to 7 and Cycle 11 onwards, and 90-day FU up to 14 months (Cycle 1 to Cycle 10 = 21 days, Cycle 11 onwards = 28 days) |  |

| End point values                     | Arm A:<br>AZD4635 +<br>durvalumab | Arm B:<br>AZD4635 +<br>durvalumab +<br>cabazitaxel |  |  |
|--------------------------------------|-----------------------------------|--|--|--|
| Subject group type                   | Reporting group                   | Reporting group                                    |  |  |
| Number of subjects analysed          | 0 <sup>[18]</sup>                 | 15   |  |  |
| Units: ng/mL                         |                                   |  |  |  |
| arithmetic mean (standard deviation) | ()                                | 483.0 (± 231.1)                                    |  |  |

Notes:

[18] - The data for Arm A was not calculated because of a patient identification risk.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Terminal half-life ( $t_{1/2\lambda z}$ )

|   |   |
|---|---|
| End point title   | Terminal half-life ( $t_{1/2\lambda z}$ ) |
| End point description:<br>Investigated the PK of AZD4635 when given in combination with durvalumab, and when given in combination with durvalumab plus cabazitaxel.   |   |
| End point type  | Secondary                                 |
| End point timeframe:<br>Arm A: Cycle 1 to 3, and Cycle 4 onwards, and 90-day follow-up (FU) visit up to 14 months [Each cycle was 28 days in length]; Arm B: Cycle 1 to 7 and Cycle 11 onwards, and 90-day FU up to 14 months (Cycle 1 to Cycle 10 = 21 days, Cycle 11 onwards = 28 days) |   |

| End point values                     | Arm A:<br>AZD4635 +<br>durvalumab | Arm B:<br>AZD4635 +<br>durvalumab +<br>cabazitaxel |  |  |
|--------------------------------------|-----------------------------------|--|--|--|
| Subject group type                   | Reporting group                   | Reporting group                                    |  |  |
| Number of subjects analysed          | 0 <sup>[19]</sup>                 | 13   |  |  |
| Units: hour (h)                      |                                   |  |  |  |
| arithmetic mean (standard deviation) | ()                                | 8.87 ( $\pm$ 4.82)                                 |  |  |

Notes:

[19] - The data for Arm A was not calculated because of a patient identification risk.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Area under the plasma concentration time curve from zero to the time of the last measurable concentration (AUClast)

|   |   |
|---|---|
| End point title   | Area under the plasma concentration time curve from zero to the time of the last measurable concentration (AUClast) |
| End point description:<br>Investigated the PK of AZD4635 when given in combination with durvalumab, and when given in combination with durvalumab plus cabazitaxel.   |   |
| End point type  | Secondary   |
| End point timeframe:<br>Arm A: Cycle 1 to 3, and Cycle 4 onwards, and 90-day follow-up (FU) visit up to 14 months [Each cycle was 28 days in length]; Arm B: Cycle 1 to 7 and Cycle 11 onwards, and 90-day FU up to 14 months (Cycle 1 to Cycle 10 = 21 days, Cycle 11 onwards = 28 days) |   |



| End point values                     | Arm A:<br>AZD4635 +<br>durvalumab | Arm B:<br>AZD4635 +<br>durvalumab +<br>cabazitaxel |  |  |
|--------------------------------------|-----------------------------------|--|--|--|
| Subject group type                   | Reporting group                   | Reporting group                                    |  |  |
| Number of subjects analysed          | 0 <sup>[20]</sup>                 | 15   |  |  |
| Units: h*ng/mL                       |                                   |  |  |  |
| arithmetic mean (standard deviation) | ()                                | 2787 (± 1056)                                      |  |  |

Notes:

[20] - The data for Arm A was not calculated because of a patient identification risk.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Area under the plasma concentration time curve from zero to 24 hours [AUC(0-24)]

|                 |  |
|-----------------|--|
| End point title | Area under the plasma concentration time curve from zero to 24 hours [AUC(0-24)] |
|-----------------|--|

End point description:

Investigated the PK of AZD4635 when given in combination with durvalumab, and when given in combination with durvalumab plus cabazitaxel.

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

End point timeframe:

Arm A: Cycle 1 to 3, and Cycle 4 onwards, and 90-day follow-up (FU) visit up to 14 months [Each cycle was 28 days in length]; Arm B: Cycle 1 to 7 and Cycle 11 onwards, and 90-day FU up to 14 months (Cycle 1 to Cycle 10 = 21 days, Cycle 11 onwards = 28 days)

| End point values                     | Arm A:<br>AZD4635 +<br>durvalumab | Arm B:<br>AZD4635 +<br>durvalumab +<br>cabazitaxel |  |  |
|--------------------------------------|-----------------------------------|--|--|--|
| Subject group type                   | Reporting group                   | Reporting group                                    |  |  |
| Number of subjects analysed          | 0 <sup>[21]</sup>                 | 14   |  |  |
| Units: h*ng/mL                       |                                   |  |  |  |
| arithmetic mean (standard deviation) | ()                                | 2874 (± 1084)                                      |  |  |

Notes:

[21] - The data for Arm A was not calculated because of a patient identification risk.

## Statistical analyses

No statistical analyses for this end point

### Secondary: Area under the plasma concentration time curve from zero extrapolated to infinity (AUCinf)

|                 |  |
|-----------------|--|
| End point title | Area under the plasma concentration time curve from zero extrapolated to infinity (AUCinf) |
|-----------------|--|

End point description:

Investigated the PK of AZD4635 when given in combination with durvalumab, and when given in combination with durvalumab plus cabazitaxel.

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

End point timeframe:

Arm A: Cycle 1 to 3, and Cycle 4 onwards, and 90-day follow-up (FU) visit up to 14 months [Each cycle was 28 days in length]; Arm B: Cycle 1 to 7 and Cycle 11 onwards, and 90-day FU up to 14 months (Cycle 1 to Cycle 10 = 21 days, Cycle 11 onwards = 28 days)

| End point values                     | Arm A:<br>AZD4635 +<br>durvalumab | Arm B:<br>AZD4635 +<br>durvalumab +<br>cabazitaxel |  |  |
|--------------------------------------|-----------------------------------|--|--|--|
| Subject group type                   | Reporting group                   | Reporting group                                    |  |  |
| Number of subjects analysed          | 0 <sup>[22]</sup>                 | 13   |  |  |
| Units: h*ng/mL                       |                                   |  |  |  |
| arithmetic mean (standard deviation) | ()                                | 3311 (± 1272)                                      |  |  |

Notes:

[22] - The data for Arm A was not calculated because of a patient identification risk.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Apparent volume of distribution during the terminal phase (V<sub>z</sub>/F)

|                 |   |
|-----------------|---|
| End point title | Apparent volume of distribution during the terminal phase (V <sub>z</sub> /F) |
|-----------------|---|

End point description:

Investigated the PK of AZD4635 when given in combination with durvalumab, and when given in combination with durvalumab plus cabazitaxel.

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

End point timeframe:

Arm A: Cycle 1 to 3, and Cycle 4 onwards, and 90-day follow-up (FU) visit up to 14 months [Each cycle was 28 days in length]; Arm B: Cycle 1 to 7 and Cycle 11 onwards, and 90-day FU up to 14 months (Cycle 1 to Cycle 10 = 21 days, Cycle 11 onwards = 28 days)

| End point values                     | Arm A:<br>AZD4635 +<br>durvalumab | Arm B:<br>AZD4635 +<br>durvalumab +<br>cabazitaxel |  |  |
|--------------------------------------|-----------------------------------|--|--|--|
| Subject group type                   | Reporting group                   | Reporting group                                    |  |  |
| Number of subjects analysed          | 0 <sup>[23]</sup>                 | 13   |  |  |
| Units: Litre (L)                     |                                   |  |  |  |
| arithmetic mean (standard deviation) | ()                                | 334.6 (± 254.4)                                    |  |  |

Notes:

[23] - The data for Arm A was not calculated because of a patient identification risk.

## Statistical analyses

**Secondary: Number of subjects with serious and non-serious adverse events**

|   |  |
|---|--|
| End point title   | Number of subjects with serious and non-serious adverse events |
| End point description:<br>Safety and tolerability of each treatment regimen were assessed in participants with mCRPC.   |  |
| End point type  | Secondary  |
| End point timeframe:<br>Arm A: From Screening up to 14 months (Each cycle was 28 days in length); Arm B: From Screening up to 14 months (Cycle 1 to Cycle 10 was 21 days in length, and Cycle 11 onwards was 28 days in length) |  |

| End point values                                      | Arm A:<br>AZD4635 +<br>durvalumab | Arm B:<br>AZD4635 +<br>durvalumab +<br>cabazitaxel |  |  |
|---|-----------------------------------|--|--|--|
| Subject group type                                    | Reporting group                   | Reporting group                                    |  |  |
| Number of subjects analysed                           | 0 <sup>[24]</sup>                 | 28   |  |  |
| Units: Participants                                   |                                   |  |  |  |
| Any Adverse Event (AE)                                |                                   | 28   |  |  |
| Any AE possibly related to treatment                  |                                   | 28   |  |  |
| Any AE possibly related to AZD4635                    |                                   | 23   |  |  |
| Any AE possibly related to Durvalumab                 |                                   | 20   |  |  |
| Any AE possibly related to Cabazitaxel                |                                   | 28   |  |  |
| Any AE of CTCAE grade 3 or higher                     |                                   | 24   |  |  |
| Any AE of CTCAE grade 3/higher<br>treatment-related   |                                   | 20   |  |  |
| Any AE of CTCAE grade 3 or higher<br>AZD4635-related  |                                   | 9  |  |  |
| Any AE of CTCAE grade 3/higher<br>Durvalumab-related  |                                   | 9  |  |  |
| Any AE of CTCAE grade 3/higher<br>Cabazitaxel-related |                                   | 19   |  |  |
| Any Adverse Event of Special Interest -<br>Durvalumab |                                   | 17   |  |  |
| Any possibly related AESI for<br>Durvalumab           |                                   | 10   |  |  |
| Any AE with outcome = death                           |                                   | 2  |  |  |
| Any AE with death possibly related to<br>treatment    |                                   | 1  |  |  |
| Any Serious Adverse Event (SAE)<br>(including death)  |                                   | 19   |  |  |
| Any SAE (including death) treatment-<br>related       |                                   | 12   |  |  |
| Any SAE leading to discontinuation of<br>AZD4635      |                                   | 4  |  |  |
| Any SAE leading to stopping of<br>AZD4635 related     |                                   | 1  |  |  |
| Any AE leading to discontinuation of<br>AZD4635       |                                   | 5  |  |  |
| Any AE leading to dose reduction of<br>AZD4635        |                                   | 4  |  |  |
| Any AE leading to dose interruption of<br>AZD4635     |                                   | 15   |  |  |

|  |  |   |  |  |
|--|--|---|--|--|
| Any AE leading to discontinuation of Durvalumab    |  | 4 |  |  |
| Any AE leading to dose interruption of Durvalumab  |  | 5 |  |  |
| Any AE leading to discontinuation of Cabazitaxel   |  | 7 |  |  |
| Any AE leading to dose reduction of Cabazitaxel    |  | 4 |  |  |
| Any AE leading to dose interruption of Cabazitaxel |  | 8 |  |  |
| Any other significant AEs                          |  | 0 |  |  |

Notes:

[24] - The data for Arm A was not calculated because of a patient identification risk.

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

All-Cause Mortality: Up to 2 years;

Serious and/or other adverse events: From Screening up to 14 months

(Each cycle was 28 days in length) for Arm A (Cycle 1 to Cycle 10 was 21 days in length, and Cycle 11 onwards was 28 days in length) for Arm B.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 24.1 |
|--------------------|------|

### Reporting groups

|                       |   |
|-----------------------|---|
| Reporting group title | Arm B: AZD4635 + durvalumab + cabazitaxel |
|-----------------------|---|

Reporting group description:

Participants received AZD4635 Dose A orally daily, durvalumab Dose B intravenously (IV) every 3 weeks (Q3W), and cabazitaxel Dose C IV Q3W

|                       |                             |
|-----------------------|-----------------------------|
| Reporting group title | Arm A: AZD4635 + durvalumab |
|-----------------------|-----------------------------|

Reporting group description:

Participants received AZD4635 Dose A orally daily, and durvalumab Dose B intravenously every 4 weeks.

| Serious adverse events                            | Arm B: AZD4635 +<br>durvalumab +<br>cabazitaxel | Arm A: AZD4635 +<br>durvalumab |  |
|---|---|--------------------------------|--|
| Total subjects affected by serious adverse events |   |                                |  |
| subjects affected / exposed                       | 19 / 28 (67.86%)                                | 2 / 2 (100.00%)                |  |
| number of deaths (all causes)                     | 7   | 2                              |  |
| number of deaths resulting from adverse events    |   |                                |  |
| Investigations                                    |   |                                |  |
| Neutrophil Count Decreased                        |   |                                |  |
| subjects affected / exposed                       | 1 / 28 (3.57%)                                  | 0 / 2 (0.00%)                  |  |
| occurrences causally related to treatment / all   | 0 / 0   | 0 / 0                          |  |
| deaths causally related to treatment / all        | 0 / 0   | 0 / 0                          |  |
| Vascular disorders                                |   |                                |  |
| Hypotension                                       |   |                                |  |
| subjects affected / exposed                       | 1 / 28 (3.57%)                                  | 0 / 2 (0.00%)                  |  |
| occurrences causally related to treatment / all   | 0 / 0   | 0 / 0                          |  |
| deaths causally related to treatment / all        | 0 / 0   | 0 / 0                          |  |
| Blood and lymphatic system disorders              |   |                                |  |
| Anaemia   |   |                                |  |

|  |                |                |  |
|--|----------------|----------------|--|
| subjects affected / exposed                          | 1 / 28 (3.57%) | 0 / 2 (0.00%)  |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Febrile Neutropenia                                  |                |                |  |
| subjects affected / exposed                          | 2 / 28 (7.14%) | 0 / 2 (0.00%)  |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Acute Post Hemorrhagic Anemia                        |                |                |  |
| subjects affected / exposed                          | 0 / 28 (0.00%) | 1 / 2 (50.00%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| General disorders and administration site conditions |                |                |  |
| Malaise  |                |                |  |
| subjects affected / exposed                          | 1 / 28 (3.57%) | 0 / 2 (0.00%)  |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Pyrexia  |                |                |  |
| subjects affected / exposed                          | 1 / 28 (3.57%) | 0 / 2 (0.00%)  |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Gastrointestinal disorders                           |                |                |  |
| Colitis  |                |                |  |
| subjects affected / exposed                          | 1 / 28 (3.57%) | 0 / 2 (0.00%)  |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Dysphagia  |                |                |  |
| subjects affected / exposed                          | 1 / 28 (3.57%) | 0 / 2 (0.00%)  |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Diarrhoea  |                |                |  |
| subjects affected / exposed                          | 1 / 28 (3.57%) | 0 / 2 (0.00%)  |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |

|   |                 |               |  |
|---|-----------------|---------------|--|
| Nausea  |                 |               |  |
| subjects affected / exposed                     | 1 / 28 (3.57%)  | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Vomiting  |                 |               |  |
| subjects affected / exposed                     | 3 / 28 (10.71%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Rectal Haemorrhage                              |                 |               |  |
| subjects affected / exposed                     | 1 / 28 (3.57%)  | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Respiratory, thoracic and mediastinal disorders |                 |               |  |
| Dyspnoea  |                 |               |  |
| subjects affected / exposed                     | 1 / 28 (3.57%)  | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Haemoptysis                                     |                 |               |  |
| subjects affected / exposed                     | 1 / 28 (3.57%)  | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Hepatobiliary disorders                         |                 |               |  |
| Cholecystitis                                   |                 |               |  |
| subjects affected / exposed                     | 1 / 28 (3.57%)  | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Cholecystitis Acute                             |                 |               |  |
| subjects affected / exposed                     | 1 / 28 (3.57%)  | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0           | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0           | 0 / 0         |  |
| Renal and urinary disorders                     |                 |               |  |
| Cystitis Haemorrhagic                           |                 |               |  |

|   |                |                |  |
|---|----------------|----------------|--|
| subjects affected / exposed                     | 1 / 28 (3.57%) | 0 / 2 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Haematuria                                      |                |                |  |
| subjects affected / exposed                     | 1 / 28 (3.57%) | 1 / 2 (50.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Hydronephrosis                                  |                |                |  |
| subjects affected / exposed                     | 1 / 28 (3.57%) | 0 / 2 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Urinary Retention                               |                |                |  |
| subjects affected / exposed                     | 1 / 28 (3.57%) | 0 / 2 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Musculoskeletal and connective tissue disorders |                |                |  |
| Myositis  |                |                |  |
| subjects affected / exposed                     | 1 / 28 (3.57%) | 0 / 2 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Arthralgia                                      |                |                |  |
| subjects affected / exposed                     | 1 / 28 (3.57%) | 0 / 2 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Infections and infestations                     |                |                |  |
| Diverticulitis                                  |                |                |  |
| subjects affected / exposed                     | 1 / 28 (3.57%) | 0 / 2 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Abscess neck                                    |                |                |  |
| subjects affected / exposed                     | 1 / 28 (3.57%) | 0 / 2 (0.00%)  |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |



|   |                |               |  |
|---|----------------|---------------|--|
| Urinary tract infection                         |                |               |  |
| subjects affected / exposed                     | 1 / 28 (3.57%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Ureteritis                                      |                |               |  |
| subjects affected / exposed                     | 1 / 28 (3.57%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |
| Metabolism and nutrition disorders              |                |               |  |
| Decreased Appetite                              |                |               |  |
| subjects affected / exposed                     | 1 / 28 (3.57%) | 0 / 2 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 0         |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0         |  |

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

| <b>Non-serious adverse events</b>                     | Arm B: AZD4635 +<br>durvalumab +<br>cabazitaxel | Arm A: AZD4635 +<br>durvalumab |  |
|---|---|--------------------------------|--|
| Total subjects affected by non-serious adverse events |   |                                |  |
| subjects affected / exposed                           | 28 / 28 (100.00%)                               | 2 / 2 (100.00%)                |  |
| Vascular disorders                                    |   |                                |  |
| Hypotension   |   |                                |  |
| subjects affected / exposed                           | 3 / 28 (10.71%)                                 | 0 / 2 (0.00%)                  |  |
| occurrences (all)                                     | 3   | 0                              |  |
| Hypertension  |   |                                |  |
| subjects affected / exposed                           | 3 / 28 (10.71%)                                 | 0 / 2 (0.00%)                  |  |
| occurrences (all)                                     | 5   | 0                              |  |
| General disorders and administration site conditions  |   |                                |  |
| Asthenia  |   |                                |  |
| subjects affected / exposed                           | 10 / 28 (35.71%)                                | 1 / 2 (50.00%)                 |  |
| occurrences (all)                                     | 15  | 1                              |  |
| Chills  |   |                                |  |
| subjects affected / exposed                           | 0 / 28 (0.00%)                                  | 1 / 2 (50.00%)                 |  |
| occurrences (all)                                     | 0   | 1                              |  |
| Fatigue   |   |                                |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| subjects affected / exposed                     | 5 / 28 (17.86%) | 2 / 2 (100.00%) |  |
| occurrences (all)                               | 7               | 2               |  |
| Pyrexia   |                 |                 |  |
| subjects affected / exposed                     | 2 / 28 (7.14%)  | 0 / 2 (0.00%)   |  |
| occurrences (all)                               | 2               | 0               |  |
| Pain  |                 |                 |  |
| subjects affected / exposed                     | 2 / 28 (7.14%)  | 0 / 2 (0.00%)   |  |
| occurrences (all)                               | 2               | 0               |  |
| Oedema peripheral                               |                 |                 |  |
| subjects affected / exposed                     | 3 / 28 (10.71%) | 0 / 2 (0.00%)   |  |
| occurrences (all)                               | 3               | 0               |  |
| Non-cardiac chest pain                          |                 |                 |  |
| subjects affected / exposed                     | 0 / 28 (0.00%)  | 1 / 2 (50.00%)  |  |
| occurrences (all)                               | 0               | 1               |  |
| Reproductive system and breast disorders        |                 |                 |  |
| Reproductive system and breast disorders        |                 |                 |  |
| subjects affected / exposed                     | 2 / 28 (7.14%)  | 0 / 2 (0.00%)   |  |
| occurrences (all)                               | 2               | 0               |  |
| Respiratory, thoracic and mediastinal disorders |                 |                 |  |
| Dyspnoea  |                 |                 |  |
| subjects affected / exposed                     | 3 / 28 (10.71%) | 1 / 2 (50.00%)  |  |
| occurrences (all)                               | 3               | 3               |  |
| Psychiatric disorders                           |                 |                 |  |
| Depression                                      |                 |                 |  |
| subjects affected / exposed                     | 3 / 28 (10.71%) | 0 / 2 (0.00%)   |  |
| occurrences (all)                               | 3               | 0               |  |
| Insomnia  |                 |                 |  |
| subjects affected / exposed                     | 3 / 28 (10.71%) | 0 / 2 (0.00%)   |  |
| occurrences (all)                               | 3               | 0               |  |
| Investigations                                  |                 |                 |  |
| Alanine aminotransferase increased              |                 |                 |  |
| subjects affected / exposed                     | 3 / 28 (10.71%) | 0 / 2 (0.00%)   |  |
| occurrences (all)                               | 4               | 0               |  |
| Amylase increased                               |                 |                 |  |

|  |                 |                 |  |
|--|-----------------|-----------------|--|
| subjects affected / exposed                    | 3 / 28 (10.71%) | 0 / 2 (0.00%)   |  |
| occurrences (all)                              | 3               | 0               |  |
| Aspartate aminotransferase increased           |                 |                 |  |
| subjects affected / exposed                    | 4 / 28 (14.29%) | 0 / 2 (0.00%)   |  |
| occurrences (all)                              | 5               | 0               |  |
| Blood alkaline phosphatase increased           |                 |                 |  |
| subjects affected / exposed                    | 4 / 28 (14.29%) | 0 / 2 (0.00%)   |  |
| occurrences (all)                              | 5               | 0               |  |
| Blood lactate dehydrogenase increased          |                 |                 |  |
| subjects affected / exposed                    | 2 / 28 (7.14%)  | 0 / 2 (0.00%)   |  |
| occurrences (all)                              | 2               | 0               |  |
| Lipase increased                               |                 |                 |  |
| subjects affected / exposed                    | 2 / 28 (7.14%)  | 0 / 2 (0.00%)   |  |
| occurrences (all)                              | 2               | 0               |  |
| Neutrophil count decreased                     |                 |                 |  |
| subjects affected / exposed                    | 4 / 28 (14.29%) | 0 / 2 (0.00%)   |  |
| occurrences (all)                              | 8               | 0               |  |
| Weight decreased                               |                 |                 |  |
| subjects affected / exposed                    | 4 / 28 (14.29%) | 2 / 2 (100.00%) |  |
| occurrences (all)                              | 7               | 2               |  |
| White blood cell count decreased               |                 |                 |  |
| subjects affected / exposed                    | 4 / 28 (14.29%) | 0 / 2 (0.00%)   |  |
| occurrences (all)                              | 7               | 0               |  |
| Injury, poisoning and procedural complications |                 |                 |  |
| Fall   |                 |                 |  |
| subjects affected / exposed                    | 2 / 28 (7.14%)  | 0 / 2 (0.00%)   |  |
| occurrences (all)                              | 3               | 0               |  |
| Nervous system disorders                       |                 |                 |  |
| Dizziness                                      |                 |                 |  |
| subjects affected / exposed                    | 5 / 28 (17.86%) | 1 / 2 (50.00%)  |  |
| occurrences (all)                              | 5               | 2               |  |
| Headache                                       |                 |                 |  |
| subjects affected / exposed                    | 3 / 28 (10.71%) | 0 / 2 (0.00%)   |  |
| occurrences (all)                              | 4               | 0               |  |
| Dysgeusia                                      |                 |                 |  |

|                                      |                  |                 |  |
|--------------------------------------|------------------|-----------------|--|
| subjects affected / exposed          | 6 / 28 (21.43%)  | 0 / 2 (0.00%)   |  |
| occurrences (all)                    | 7                | 0               |  |
| Neuropathy peripheral                |                  |                 |  |
| subjects affected / exposed          | 2 / 28 (7.14%)   | 0 / 2 (0.00%)   |  |
| occurrences (all)                    | 2                | 0               |  |
| Peripheral sensory neuropathy        |                  |                 |  |
| subjects affected / exposed          | 3 / 28 (10.71%)  | 0 / 2 (0.00%)   |  |
| occurrences (all)                    | 4                | 0               |  |
| Blood and lymphatic system disorders |                  |                 |  |
| Anaemia                              |                  |                 |  |
| subjects affected / exposed          | 14 / 28 (50.00%) | 1 / 2 (50.00%)  |  |
| occurrences (all)                    | 19               | 4               |  |
| Neutropenia                          |                  |                 |  |
| subjects affected / exposed          | 6 / 28 (21.43%)  | 0 / 2 (0.00%)   |  |
| occurrences (all)                    | 12               | 0               |  |
| Thrombocytopenia                     |                  |                 |  |
| subjects affected / exposed          | 2 / 28 (7.14%)   | 0 / 2 (0.00%)   |  |
| occurrences (all)                    | 2                | 0               |  |
| Gastrointestinal disorders           |                  |                 |  |
| Abdominal pain                       |                  |                 |  |
| subjects affected / exposed          | 4 / 28 (14.29%)  | 1 / 2 (50.00%)  |  |
| occurrences (all)                    | 5                | 1               |  |
| Constipation                         |                  |                 |  |
| subjects affected / exposed          | 8 / 28 (28.57%)  | 1 / 2 (50.00%)  |  |
| occurrences (all)                    | 8                | 1               |  |
| Diarrhoea                            |                  |                 |  |
| subjects affected / exposed          | 14 / 28 (50.00%) | 2 / 2 (100.00%) |  |
| occurrences (all)                    | 21               | 4               |  |
| Dyspepsia                            |                  |                 |  |
| subjects affected / exposed          | 4 / 28 (14.29%)  | 0 / 2 (0.00%)   |  |
| occurrences (all)                    | 5                | 0               |  |
| Dry mouth                            |                  |                 |  |
| subjects affected / exposed          | 2 / 28 (7.14%)   | 0 / 2 (0.00%)   |  |
| occurrences (all)                    | 2                | 0               |  |
| Gastrooesophageal reflux disease     |                  |                 |  |

|  |                                   |                                |  |
|--|-----------------------------------|--------------------------------|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p>  | <p>2 / 28 (7.14%)</p> <p>2</p>    | <p>1 / 2 (50.00%)</p> <p>1</p> |  |
| <p>Oral pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>   | <p>2 / 28 (7.14%)</p> <p>2</p>    | <p>0 / 2 (0.00%)</p> <p>0</p>  |  |
| <p>Nausea</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>  | <p>17 / 28 (60.71%)</p> <p>20</p> | <p>1 / 2 (50.00%)</p> <p>1</p> |  |
| <p>Vomiting</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>  | <p>9 / 28 (32.14%)</p> <p>12</p>  | <p>0 / 2 (0.00%)</p> <p>0</p>  |  |
| <p>Skin and subcutaneous tissue disorders</p> <p>Dry skin</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>            | <p>2 / 28 (7.14%)</p> <p>2</p>    | <p>0 / 2 (0.00%)</p> <p>0</p>  |  |
| <p>Pruritus</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>  | <p>0 / 28 (0.00%)</p> <p>0</p>    | <p>1 / 2 (50.00%)</p> <p>3</p> |  |
| <p>Renal and urinary disorders</p> <p>Haematuria</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>                     | <p>5 / 28 (17.86%)</p> <p>7</p>   | <p>0 / 2 (0.00%)</p> <p>0</p>  |  |
| <p>Urinary retention</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>   | <p>0 / 28 (0.00%)</p> <p>0</p>    | <p>1 / 2 (50.00%)</p> <p>1</p> |  |
| <p>Musculoskeletal and connective tissue disorders</p> <p>Arthralgia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>9 / 28 (32.14%)</p> <p>11</p>  | <p>0 / 2 (0.00%)</p> <p>0</p>  |  |
| <p>Back pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>   | <p>5 / 28 (17.86%)</p> <p>5</p>   | <p>1 / 2 (50.00%)</p> <p>1</p> |  |
| <p>Flank pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>  | <p>2 / 28 (7.14%)</p> <p>2</p>    | <p>0 / 2 (0.00%)</p> <p>0</p>  |  |
| <p>Muscle spasms</p>   |                                   |                                |  |

|                                    |                 |                 |  |
|------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed        | 2 / 28 (7.14%)  | 0 / 2 (0.00%)   |  |
| occurrences (all)                  | 2               | 0               |  |
| Muscular weakness                  |                 |                 |  |
| subjects affected / exposed        | 3 / 28 (10.71%) | 0 / 2 (0.00%)   |  |
| occurrences (all)                  | 6               | 0               |  |
| Myalgia                            |                 |                 |  |
| subjects affected / exposed        | 2 / 28 (7.14%)  | 0 / 2 (0.00%)   |  |
| occurrences (all)                  | 2               | 0               |  |
| Pain in extremity                  |                 |                 |  |
| subjects affected / exposed        | 3 / 28 (10.71%) | 0 / 2 (0.00%)   |  |
| occurrences (all)                  | 4               | 0               |  |
| Infections and infestations        |                 |                 |  |
| Urinary tract infection            |                 |                 |  |
| subjects affected / exposed        | 6 / 28 (21.43%) | 1 / 2 (50.00%)  |  |
| occurrences (all)                  | 7               | 2               |  |
| Metabolism and nutrition disorders |                 |                 |  |
| Hyperglycaemia                     |                 |                 |  |
| subjects affected / exposed        | 3 / 28 (10.71%) | 0 / 2 (0.00%)   |  |
| occurrences (all)                  | 3               | 0               |  |
| Decreased appetite                 |                 |                 |  |
| subjects affected / exposed        | 7 / 28 (25.00%) | 2 / 2 (100.00%) |  |
| occurrences (all)                  | 8               | 2               |  |
| Hyperkalaemia                      |                 |                 |  |
| subjects affected / exposed        | 2 / 28 (7.14%)  | 0 / 2 (0.00%)   |  |
| occurrences (all)                  | 4               | 0               |  |
| Hyperuricaemia                     |                 |                 |  |
| subjects affected / exposed        | 3 / 28 (10.71%) | 0 / 2 (0.00%)   |  |
| occurrences (all)                  | 3               | 0               |  |
| Hypocalcaemia                      |                 |                 |  |
| subjects affected / exposed        | 2 / 28 (7.14%)  | 0 / 2 (0.00%)   |  |
| occurrences (all)                  | 3               | 0               |  |
| Hypokalaemia                       |                 |                 |  |
| subjects affected / exposed        | 2 / 28 (7.14%)  | 0 / 2 (0.00%)   |  |
| occurrences (all)                  | 4               | 0               |  |
| Hypophosphataemia                  |                 |                 |  |

|                             |                 |               |  |
|-----------------------------|-----------------|---------------|--|
| subjects affected / exposed | 3 / 28 (10.71%) | 0 / 2 (0.00%) |  |
| occurrences (all)           | 4               | 0             |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date              | Amendment   |
|-------------------|---|
| 07 September 2020 | The global protocol was amended to address comments received from various health authorities in the EU. |
| 24 November 2020  | The global protocol was amended due to the Sponsor's decision to close enrolment in Arm A.              |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The arbitrary value 9999.9999 indicates that the parameter was not measured.

Notes: