



## Clinical trial results:

**A multicentre, open-label, single-arm, molecular profiling study of patients with epidermal growth factor receptor (EGFR) mutation-positive locally advanced or metastatic non-small-cell lung cancer (NSCLC) treated with osimertinib**

### Summary

|                          |                   |
|--------------------------|-------------------|
| EudraCT number           | 2017-002359-27    |
| Trial protocol           | ES IT             |
| Global end of trial date | 19 September 2023 |

### Results information

|                                |   |
|--------------------------------|---|
| Result version number          | v2 (current)  |
| This version publication date  | 30 October 2024   |
| First version publication date | 19 September 2024   |
| Version creation reason        | <ul style="list-style-type: none"><li>• Correction of full data set</li><li>• Correction of information</li></ul> |

### Trial information

#### Trial identification

|                       |             |
|-----------------------|-------------|
| Sponsor protocol code | D5161C00003 |
|-----------------------|-------------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT03239340 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | AstraZeneca  |
| Sponsor organisation address | Södertälje, Södertälje, Sweden, 151 85   |
| Public contact               | Global Clinical Lead, AstraZeneca, +1 8772409479, information.center@astrazeneca.com |
| Scientific contact           | Global Clinical Lead, AstraZeneca, +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                       | 18 July 2023      |
| Is this the analysis of the primary completion data? | No                |
| Global end of trial reached?                         | Yes               |
| Global end of trial date                             | 19 September 2023 |
| Was the trial ended prematurely?                     | No                |

Notes:

## General information about the trial

Main objective of the trial:

To examine the tumour genetic and proteomic profile at the point of disease progression in patients receiving osimertinib as first-line epidermal growth factor receptor (EGFR) TKI therapy for EGFRm+ locally advanced or metastatic non-small-cell lung cancer (NSCLC) compared to the profile prior to initiation of treatment.

Protection of trial subjects:

The study was performed in accordance with ethical principles that had their origin in the Declaration of Helsinki and were consistent with International Council of Harmonisation Good Clinical Practice and the AstraZeneca policy on Bioethics and Human Biological Samples applicable laws and regulatory requirements.

Background therapy: -

Evidence for comparator: -

|   |             |
|---|-------------|
| Actual start date of recruitment                          | 30 May 2018 |
| 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 | Italy: 11              |
| Country: Number of subjects enrolled | Korea, Republic of: 65 |
| Country: Number of subjects enrolled | Malaysia: 50           |
| Country: Number of subjects enrolled | Spain: 16              |
| Country: Number of subjects enrolled | United States: 12      |
| Worldwide total number of subjects   | 154                    |
| EEA total number of subjects         | 27                     |

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)      | 83 |
| From 65 to 84 years       | 70 |
| 85 years and over         | 1  |

## Subject disposition

### Recruitment

Recruitment details:

Participants were enrolled in this study from 30 May 2018 (First subject in) and analyses presented in this results form are based on a data cut-off of 18 July 2023.

### Pre-assignment

Screening details:

Participants meeting eligibility criteria predefined in protocol were enrolled in the study. All the assessments were performed as per the schedule of the assessments.

### Period 1

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

### Arms

|           |                  |
|-----------|------------------|
| Arm title | Osimertinib 80mg |
|-----------|------------------|

Arm description:

Participants received Osimertinib 80mg orally once daily.

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

Dosage and administration details:

Participants received 80 mg Osimertinib orally once daily

| Number of subjects in period 1               | Osimertinib 80mg |
|--|------------------|
| Started                                      | 154              |
| Completed                                    | 33               |
| Not completed                                | 121              |
| Physician decision                           | 16               |
| Lost to follow-up                            | 2                |
| Patients who are ongoing in the study at DCO | 10               |
| Death  | 40               |
| Other  | 26               |
| Withdrawal by Subject                        | 27               |

## Baseline characteristics

### Reporting groups

|                       |                  |
|-----------------------|------------------|
| Reporting group title | Osimertinib 80mg |
|-----------------------|------------------|

Reporting group description:

Participants received Osimertinib 80mg orally once daily.

| Reporting group values                             | Osimertinib 80mg | Total |  |
|--|------------------|-------|--|
| Number of subjects                                 | 154              | 154   |  |
| Age categorical                                    |                  |       |  |
| Units: Subjects                                    |                  |       |  |
| 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     |  |
| Adults (<50)                                       | 18               | 18    |  |
| >=50 - <65   | 65               | 65    |  |
| >=65 - <75   | 50               | 50    |  |
| >=75   | 21               | 21    |  |
| Age Continuous                                     |                  |       |  |
| Units: years                                       |                  |       |  |
| arithmetic mean                                    | 62.7             |       |  |
| standard deviation                                 | ± 10.36          | -     |  |
| Sex: Female, Male                                  |                  |       |  |
| Units: Participants                                |                  |       |  |
| Female   | 92               | 92    |  |
| Male   | 62               | 62    |  |
| Race/Ethnicity, Customized                         |                  |       |  |
| Units: Subjects                                    |                  |       |  |
| White  | 30               | 30    |  |
| Black or African American                          | 5                | 5     |  |
| Asian  | 118              | 118   |  |
| Other  | 1                | 1     |  |
| Race/Ethnicity, Customized                         |                  |       |  |
| Units: Subjects                                    |                  |       |  |
| Hispanic   | 6                | 6     |  |
| Not Hispanic or Latino                             | 148              | 148   |  |

### Subject analysis sets

|                            |  |
|----------------------------|--|
| Subject analysis set title | Exon19del- EGFR tumor mutation at baseline |
|----------------------------|--|

|                           |               |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

Subject analysis set description:

Participants with Exon19del received Osimertinib 80mg orally once daily.

|                            |  |
|----------------------------|--|
| Subject analysis set title | L858R- EGFR tumor mutation at baseline |
|----------------------------|--|

|                           |               |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

Subject analysis set description:

Participants with L858R received Osimertinib 80mg orally once daily

|                            |   |
|----------------------------|---|
| Subject analysis set title | Exon19del- Detectable in plasma ctDNA at baseline |
| Subject analysis set type  | Full analysis                                     |

Subject analysis set description:

Participants with Exon19del received Osimertinib 80mg orally once daily

|                            |  |
|----------------------------|--|
| Subject analysis set title | L858R-Detectable in plasma ctDNA at baseline |
| Subject analysis set type  | Full analysis                                |

Subject analysis set description:

Participants with L858R received Osimertinib 80mg orally once daily

| Reporting group values                             | Exon19del- EGFR tumor mutation at baseline | L858R- EGFR tumor mutation at baseline | Exon19del- Detectable in plasma ctDNA at baseline |
|--|--|--|---|
| Number of subjects                                 | 85   | 58                                     | 62  |
| Age categorical<br>Units: Subjects                 |  |  |   |
| 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                                      |   |
| Adults (<50)                                       | 11   | 5                                      |   |
| >=50 - <65   | 41   | 23                                     |   |
| >=65 - <75   | 21   | 22                                     |   |
| >=75   | 12   | 8                                      |   |
| Age Continuous<br>Units: years                     |  |  |   |
| arithmetic mean                                    | 61.6                                       | 63.8                                   |   |
| standard deviation                                 | ± 10.74                                    | ± 9.51                                 | ±   |
| Sex: Female, Male<br>Units: Participants           |  |  |   |
| Female   | 34   | 23                                     |   |
| Male   | 51   | 35                                     |   |
| Race/Ethnicity, Customized<br>Units: Subjects      |  |  |   |
| White  | 11   | 17                                     |   |
| Black or African American                          | 4  | 0                                      |   |
| Asian  | 69   | 41                                     |   |
| Other  | 1  | 0                                      |   |
| Race/Ethnicity, Customized<br>Units: Subjects      |  |  |   |
| Hispanic   | 3  | 3                                      |   |
| Not Hispanic or Latino                             | 82   | 55                                     |   |

| Reporting group values             | L858R-Detectable in plasma ctDNA at baseline |  |  |
|------------------------------------|--|--|--|
| Number of subjects                 | 46   |  |  |
| Age categorical<br>Units: Subjects |  |  |  |

|  |   |  |  |
|--|---|--|--|
| Preterm newborn infants<br>(gestational age < 37 wks)<br>Newborns (0-27 days)<br>Infants and toddlers (28 days-23 months)<br>Children (2-11 years)<br>Adults (<50)<br>>=50 - <65<br>>=65 - <75<br>>=75 |   |  |  |
| Age Continuous<br>Units: years<br>arithmetic mean<br>standard deviation  | ± |  |  |
| Sex: Female, Male<br>Units: Participants   |   |  |  |
| Female<br>Male   |   |  |  |
| Race/Ethnicity, Customized<br>Units: Subjects  |   |  |  |
| White<br>Black or African American<br>Asian<br>Other   |   |  |  |
| Race/Ethnicity, Customized<br>Units: Subjects  |   |  |  |
| Hispanic<br>Not Hispanic or Latino   |   |  |  |

## End points

### End points reporting groups

|   |   |
|---|---|
| Reporting group title   | Osimertinib 80mg                                  |
| Reporting group description:<br>Participants received Osimertinib 80mg orally once daily.                     |   |
| Subject analysis set title  | Exon19del- EGFR tumor mutation at baseline        |
| Subject analysis set type   | Full analysis                                     |
| Subject analysis set description:<br>Participants with Exon19del received Osimertinib 80mg orally once daily. |   |
| Subject analysis set title  | L858R- EGFR tumor mutation at baseline            |
| Subject analysis set type   | Full analysis                                     |
| Subject analysis set description:<br>Participants with L858R received Osimertinib 80mg orally once daily      |   |
| Subject analysis set title  | Exon19del- Detectable in plasma ctDNA at baseline |
| Subject analysis set type   | Full analysis                                     |
| Subject analysis set description:<br>Participants with Exon19del received Osimertinib 80mg orally once daily  |   |
| Subject analysis set title  | L858R-Detectable in plasma ctDNA at baseline      |
| Subject analysis set type   | Full analysis                                     |
| Subject analysis set description:<br>Participants with L858R received Osimertinib 80mg orally once daily      |   |

### Primary: Proportion of patients with a given tumour genetic and proteomic marker at the point of disease progression

|  |  |
|--|--|
| End point title  | Proportion of patients with a given tumour genetic and proteomic marker at the point of disease progression <sup>[1]</sup> |
| End point description:<br>The frequency of genetic and proteomic markers at disease progression regardless of their prevalence was evaluated. The primary analysis set included all patients with evaluable paired biopsies, which were defined as follows: the first biopsy was taken prior to osimertinib treatment, and the second biopsy was taken at any time between Investigator-assessed RECIST 1.1-defined progression and before the start of any new anticancer treatment. The primary analysis set was included for the analysis for the endpoint. |  |
| End point type   | Primary  |
| End point timeframe:<br>Genetic and proteomic markers were assessed at baseline and progression (up to 5 years after baseline)   |  |

Notes:

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

Justification: No statistical analysis was calculated for the Outcome measure

| End point values                                  | Osimertinib 80mg    |  |  |  |
|---|---------------------|--|--|--|
| Subject group type                                | Reporting group     |  |  |  |
| Number of subjects analysed                       | 51                  |  |  |  |
| Units: Percentage of participants                 |                     |  |  |  |
| number (confidence interval 95%)                  |                     |  |  |  |
| AKT2; Copy Number Alteration: Type; amplification | 2.0 (0.05 to 10.45) |  |  |  |
| ALK; Rearrangement                                | 3.9 (0.48 to 13.46) |  |  |  |
| APC; Copy Number Alteration; Type: loss           | 2.0 (0.05 to 10.45) |  |  |  |



|   |                      |  |  |  |
|---|----------------------|--|--|--|
| ARAF; Copy Number Alteration; Type: amplification   | 3.9 (0.48 to 13.46)  |  |  |  |
| ASXL1; Short Variant; Type: Q588*                   | 2.0 (0.05 to 10.45)  |  |  |  |
| ATRX; Short Variant; Type: P599fs*22                | 2.0 (0.05 to 10.45)  |  |  |  |
| AXL; Copy Number Alteration; Type: amplification    | 2.0 (0.05 to 10.45)  |  |  |  |
| BCL2L2; Copy Number Alteration; Type: amplification | 3.9 (0.48 to 13.46)  |  |  |  |
| BRAF; Rearrangement                                 | 2.0 (0.05 to 10.45)  |  |  |  |
| BRAF; Short variant; Type: G469A                    | 2.0 (0.05 to 10.45)  |  |  |  |
| BRAF; Short variant Type: V600E                     | 3.9 (0.48 to 13.46)  |  |  |  |
| CBL; Short Variant; Type: R149Q                     | 2.0 (0.05 to 10.45)  |  |  |  |
| CCND1 Copy Number Alteration Type: amplification    | 3.9 (0.48 to 13.46)  |  |  |  |
| CCNE1 Copy Number Alteration Type: amplification    | 5.9 (1.23 to 16.24)  |  |  |  |
| CDK4 Copy Number Alteration Type: amplification     | 2.0 (0.05 to 10.45)  |  |  |  |
| CDK6 Copy Number Alteration Type: amplification     | 2.0 (0.05 to 10.45)  |  |  |  |
| CDKN1B Short Variant Type: S2*                      | 2.0 (0.05 to 10.45)  |  |  |  |
| CDKN2A Copy Number Alteration Type: loss            | 15.7 (7.02 to 28.59) |  |  |  |
| CDKN2A; Short Variant Type: P38L                    | 2.0 (0.05 to 10.45)  |  |  |  |
| CDKN2B Copy Number Alteration Type: loss            | 15.7 (7.02 to 28.59) |  |  |  |
| CRKL Copy Number Alteration Type: amplification     | 2.0 (0.05 to 10.45)  |  |  |  |
| CUL4A Copy Number Alteration Type: amplification    | 2.0 (0.05 to 10.45)  |  |  |  |
| DIS3 Copy Number Alteration Type: amplification     | 2.0 (0.05 to 10.45)  |  |  |  |
| EGFR Copy Number Alteration Type: amplification     | 11.8 (4.44 to 23.87) |  |  |  |
| EGFR Rearrangement                                  | 2.0 (0.05 to 10.45)  |  |  |  |
| EGFR Short Variant Type: C797S                      | 13.7 (5.70 to 26.26) |  |  |  |
| EGFR Short Variant Type: L858R                      | 2.0 (0.05 to 10.45)  |  |  |  |
| EMSY Copy Number Alteration Type: amplification     | 2.0 (0.05 to 10.45)  |  |  |  |
| ERBB2 Copy Number Alteration Type: amplification    | 2.0 (0.05 to 10.45)  |  |  |  |
| FANCG Rearrangement                                 | 2.0 (0.05 to 10.45)  |  |  |  |
| FGF10 Copy Number Alteration Type: amplification    | 3.9 (0.48 to 13.46)  |  |  |  |
| FGF14; Copy Number Alteration; Type: amplification  | 2.0 (0.05 to 10.45)  |  |  |  |
| FGF19 Copy Number Alteration Type: amplification    | 2.0 (0.05 to 10.45)  |  |  |  |
| FGFR1 Copy Number Alteration Type: amplification    | 2.0 (0.05 to 10.45)  |  |  |  |

|   |                      |  |  |  |
|---|----------------------|--|--|--|
| FGFR3 Rearrangement                               | 2.0 (0.05 to 10.45)  |  |  |  |
| FGFR4 Copy Number Alteration Type: amplification  | 2.0 (0.05 to 10.45)  |  |  |  |
| HGF Copy Number Alteration Type: amplification    | 3.9 (0.48 to 13.46)  |  |  |  |
| HRAS Short Variant Type: Q61R                     | 2.0 (0.05 to 10.45)  |  |  |  |
| IDH1 Short Variant Type: R132L                    | 2.0 (0.05 to 10.45)  |  |  |  |
| IGF1R Copy Number Alteration Type: amplification  | 2.0 (0.05 to 10.45)  |  |  |  |
| IRS2 Copy Number Alteration Type: amplification   | 2.0 (0.05 to 10.45)  |  |  |  |
| KRAS Copy Number Alteration Type: amplification   | 3.9 (0.48 to 13.46)  |  |  |  |
| LYN Copy Number Alteration Type: amplification    | 2.0 (0.05 to 10.45)  |  |  |  |
| MAP2K1 Short Variant Type: E102_I103del           | 2.0 (0.05 to 10.45)  |  |  |  |
| MCL1 Copy Number Alteration Type: amplification   | 5.9 (1.23 to 16.24)  |  |  |  |
| MDM2 Copy Number Alteration Type: amplification   | 2.0 (0.05 to 10.45)  |  |  |  |
| MET Copy Number Alteration Type: amplification    | 17.6 (8.40 to 30.87) |  |  |  |
| MTAP Copy Number Alteration Type: loss            | 13.7 (5.70 to 26.26) |  |  |  |
| MYC Copy Number Alteration Type: amplification    | 3.9 (0.48 to 13.46)  |  |  |  |
| MYCN Copy Number Alteration Type: amplification   | 2.0 (0.05 to 10.45)  |  |  |  |
| NF1 Short Variant Type: M1I                       | 2.0 (0.05 to 10.45)  |  |  |  |
| NFE2L2 Short Variant Type: D29N                   | 2.0 (0.05 to 10.45)  |  |  |  |
| NFKBIA Copy Number Alteration Type: amplification | 9.8 (3.26 to 21.41)  |  |  |  |
| NKX2-1 Copy Number Alteration Type: amplification | 9.8 (3.26 to 21.41)  |  |  |  |
| NOTCH3 Rearrangement                              | 2.0 (0.05 to 10.45)  |  |  |  |
| NTRK1 Copy Number Alteration Type: amplification  | 3.9 (0.48 to 13.46)  |  |  |  |
| PARP1 Copy Number Alteration Type: amplification  | 2.0 (0.05 to 10.45)  |  |  |  |
| PDGFRB Copy Number Alteration Type: amplification | 2.0 (0.05 to 10.45)  |  |  |  |
| PIK3CA Short Variant Type: E542K                  | 2.0 (0.05 to 10.45)  |  |  |  |
| PIM1 Copy Number Alteration Type: amplification   | 2.0 (0.05 to 10.45)  |  |  |  |
| RAD21 Copy Number Alteration Type: amplification  | 3.9 (0.48 to 13.46)  |  |  |  |
| RB1 Copy Number Alteration Type: loss             | 3.9 (0.48 to 13.46)  |  |  |  |
| RB1 Short Variant Type: Q846*                     | 2.0 (0.05 to 10.45)  |  |  |  |
| RICTOR Copy Number Alteration Type: amplification | 7.8 (2.18 to 18.88)  |  |  |  |
| SMAD4 Rearrangement                               | 2.0 (0.05 to 10.45)  |  |  |  |

|  |                     |  |  |  |
|--|---------------------|--|--|--|
| SMAD4 Short Variant Type: W524L                    | 2.0 (0.05 to 10.45) |  |  |  |
| SPEN Short Variant Type: D2047fs*17                | 2.0 (0.05 to 10.45) |  |  |  |
| STK11 Copy Number Alteration Type: loss            | 2.0 (0.05 to 10.45) |  |  |  |
| STK11 Short Variant Type: K269fs*18                | 2.0 (0.05 to 10.45) |  |  |  |
| TERC Copy Number Alteration Type: amplification    | 2.0 (0.05 to 10.45) |  |  |  |
| TERT Short Variant Type: promoter - 146C>T         | 2.0 (0.05 to 10.45) |  |  |  |
| TET2 Short Variant Type: Q916*                     | 2.0 (0.05 to 10.45) |  |  |  |
| TET2 Short Variant Type: V1862fs*13                | 2.0 (0.05 to 10.45) |  |  |  |
| TP53 Short Variant Type: R213*                     | 2.0 (0.05 to 10.45) |  |  |  |
| WHSC1L1 Copy Number Alteration Type: amplification | 3.9 (0.48 to 13.46) |  |  |  |
| ZNF703 Copy Number Alteration Type: amplification  | 3.9 (0.48 to 13.46) |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Progression free survival (PFS)

|   |                                 |
|---|---------------------------------|
| End point title   | Progression free survival (PFS) |
| End point description:  |                                 |
| PFS is defined as the time from first dose of osimertinib until the date of Investigator assessed Response Evaluation Criteria in Solid Tumours (RECIST) 1.1-defined progression or death (by any cause in the absence of progression) regardless of whether the patient withdraws from therapy or receives another anticancer therapy prior to progression. The full analysis set included all patients who received at least one dose of Osimertinib. |                                 |
| End point type  | Secondary                       |
| End point timeframe:  |                                 |
| From date of first dose until date of progression or death (by any cause in the absence of recurrence), up to 5 years   |                                 |

|                                  |                     |  |  |  |
|----------------------------------|---------------------|--|--|--|
| <b>End point values</b>          | Osimertinib 80mg    |  |  |  |
| Subject group type               | Reporting group     |  |  |  |
| Number of subjects analysed      | 154                 |  |  |  |
| Units: Months                    |                     |  |  |  |
| median (confidence interval 95%) | 16.4 (12.7 to 20.3) |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Objective Response Rate (ORR)

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

End point description:

ORR is defined as the number (%) of patients with at least one visit response of complete response (CR) or partial response (PR) that is confirmed at least 4 weeks later. The full analysis set included all patients who received at least one dose of Osimertinib.

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

End point timeframe:

From date of first dose until progression, or last evaluable assessment in the absence of progression, up to 5 years

|                                   |                          |  |  |  |
|-----------------------------------|--------------------------|--|--|--|
| <b>End point values</b>           | Osimertinib<br>80mg      |  |  |  |
| Subject group type                | Reporting group          |  |  |  |
| Number of subjects analysed       | 154                      |  |  |  |
| Units: Percentage of participants |                          |  |  |  |
| number (confidence interval 95%)  | 73.4 (65.66 to<br>80.17) |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Duration of Response (DoR)

|                 |                            |
|-----------------|----------------------------|
| End point title | Duration of Response (DoR) |
|-----------------|----------------------------|

End point description:

Duration of response is defined as the time from the date of first documented response, (that is subsequently confirmed) until date of documented progression or death in the absence of disease progression, the end of response should coincide with the date of progression or death from any cause used for the PFS endpoint. The time of the initial response will be defined as the latest of the dates contributing towards the first visit that was CR or PR that was subsequently confirmed. The full analysis set included all patients who received at least one dose of Osimertinib. The Duration of response is calculated for only participants with a confirmed response. Participants must have had measurable disease at baseline to be included in the study.

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

End point timeframe:

From date of first documentation of complete/partial response until the date of progression, or last evaluable RECIST assessment for participants that did not progress within 2 missed visits of last assessment, up to 5 years

|                                  |                        |  |  |  |
|----------------------------------|------------------------|--|--|--|
| <b>End point values</b>          | Osimertinib<br>80mg    |  |  |  |
| Subject group type               | Reporting group        |  |  |  |
| Number of subjects analysed      | 113                    |  |  |  |
| Units: Months                    |                        |  |  |  |
| median (confidence interval 95%) | 18.8 (14.2 to<br>22.3) |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Disease control rate (DCR)

|  |                            |
|--|----------------------------|
| End point title  | Disease control rate (DCR) |
| End point description:   |                            |
| DCR is defined as percentage of patients with confirmed complete response, confirmed partial response or with stable disease. The full analysis set included all patients who received at least one dose of Osimertinib. |                            |
| End point type   | Secondary                  |
| End point timeframe:   |                            |
| 8 weeks  |                            |

|                                   |                          |  |  |  |
|-----------------------------------|--------------------------|--|--|--|
| <b>End point values</b>           | Osimertinib<br>80mg      |  |  |  |
| Subject group type                | Reporting group          |  |  |  |
| Number of subjects analysed       | 154                      |  |  |  |
| Units: Percentage of participants |                          |  |  |  |
| number (confidence interval 95%)  | 94.8 (90.02 to<br>97.73) |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Time to Treatment Discontinuation or Death (TTD)

|   |  |
|---|--|
| End point title   | Time to Treatment Discontinuation or Death (TTD) |
| End point description:  |  |
| TTD is defined as the time from the date of first dose of osimertinib to the earliest of treatment discontinuation or death. The full analysis set included all patients who received at least one dose of osimertinib. |  |
| End point type  | Secondary  |
| End point timeframe:  |  |
| From date of first dose to treatment discontinuation or death (by any cause in the absence of recurrence), up to 5 years  |  |

| End point values                 | Osimertinib<br>80mg    |  |  |  |
|----------------------------------|------------------------|--|--|--|
| Subject group type               | Reporting group        |  |  |  |
| Number of subjects analysed      | 154                    |  |  |  |
| Units: Months                    |                        |  |  |  |
| median (confidence interval 95%) | 20.0 (16.3 to<br>23.8) |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Time to first subsequent therapy or Death (TFST)

|  |  |
|--|--|
| End point title  | Time to first subsequent therapy or Death (TFST) |
| End point description:<br>TFST is defined as the time from the date of first dose of Osimertinib to the earlier of the date of anticancer therapy start date following study treatment discontinuation, or death. The full analysis set included all patients who received at least one dose of Osimertinib. |  |
| End point type   | Secondary  |
| End point timeframe:<br>From date of first dose to start of subsequent anticancer therapy or death (by any cause in the absence of recurrence), up to 5 years  |  |

| End point values                 | Osimertinib<br>80mg    |  |  |  |
|----------------------------------|------------------------|--|--|--|
| Subject group type               | Reporting group        |  |  |  |
| Number of subjects analysed      | 154                    |  |  |  |
| Units: Months                    |                        |  |  |  |
| median (confidence interval 95%) | 32.1 (24.0 to<br>47.7) |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: PFS in patient subgroups defined by molecular profile: Epidermal growth factor receptor (EGFR) tumor mutation at baseline

|   |   |
|---|---|
| End point title   | PFS in patient subgroups defined by molecular profile:<br>Epidermal growth factor receptor (EGFR) tumor mutation at<br>baseline |
| End point description:<br>PFS is defined as the time from first dose of osimertinib until the date of Investigator assessed Response Evaluation Criteria in Solid Tumours (RECIST) 1.1-defined progression or death (by any cause in the absence of progression) regardless of whether the patient withdraws from therapy or receives another |   |

anticancer therapy prior to progression. PFS was analysed in patient subgroups defined by molecular profile, including but not limited to: EGFR tumor mutation at baseline-Exon19del or L858R. The full analysis set included all patients who received at least one dose of Osimertinib.

|   |           |
|---|-----------|
| End point type  | Secondary |
| End point timeframe:  |           |
| From date of first dose until date of progression or death (by any cause in the absence of recurrence), up to 5 years |           |

|                                  |  |  |  |  |
|----------------------------------|--|--|--|--|
| <b>End point values</b>          | Exon19del- EGFR tumor mutation at baseline | L858R- EGFR tumor mutation at baseline |  |  |
| Subject group type               | Subject analysis set                       | Subject analysis set                   |  |  |
| Number of subjects analysed      | 85   | 58                                     |  |  |
| Units: Months                    |  |  |  |  |
| median (confidence interval 95%) | 22.0 (16.0 to 27.6)                        | 12.9 (10.8 to 18.2)                    |  |  |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: PFS in patient subgroups defined by molecular profile: Detectable in plasma derived ctDNA at baseline**

|                 |   |
|-----------------|---|
| End point title | PFS in patient subgroups defined by molecular profile: Detectable in plasma derived ctDNA at baseline |
|-----------------|---|

End point description:

PFS is defined as the time from first dose of osimertinib until the date of Investigator assessed Response Evaluation Criteria in Solid Tumours (RECIST) 1.1-defined progression or death (by any cause in the absence of progression) regardless of whether the patient withdraws from therapy or receives another anticancer therapy prior to progression. PFS was analysed in patient subgroups defined by molecular profile, including but not limited to: Exon19del or L858R detectable in plasma derived circulating tumour deoxyribonucleic acid (ctDNA) at baseline. The full analysis set included all patients who received at least 1 dose of Osimertinib.

|   |           |
|---|-----------|
| End point type  | Secondary |
| End point timeframe:  |           |
| From date of first dose until date of progression or death (by any cause in the absence of recurrence), up to 5 years |           |

|                                  |   |   |  |  |
|----------------------------------|---|---|--|--|
| <b>End point values</b>          | Exon19del- Detectable in plasma ctDNA at baseline | L858R- Detectable in plasma ctDNA at baseline |  |  |
| Subject group type               | Subject analysis set                              | Subject analysis set                          |  |  |
| Number of subjects analysed      | 62  | 46  |  |  |
| Units: Months                    |   |   |  |  |
| median (confidence interval 95%) | 19.6 (12.7 to 24.0)                               | 13.7 (9.0 to 18.2)                            |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: ORR in patient subgroups defined by molecular profile: EGFR tumor mutation at baseline

|                 |  |
|-----------------|--|
| End point title | ORR in patient subgroups defined by molecular profile: EGFR tumor mutation at baseline |
|-----------------|--|

End point description:

ORR is defined as the number (%) of patients with at least one visit response of complete response or partial response that is confirmed at least 4 weeks later. ORR was analysed in patient subgroups defined by molecular profile: EGFR tumor mutation at baseline-Exon19del or L858R. The full analysis set included all patients who received at least 1 dose of Osimertinib.

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

End point timeframe:

From date of first dose until progression, or last evaluable assessment in the absence of progression, up to 5 years

| End point values                  | Exon19del- EGFR tumor mutation at baseline | L858R- EGFR tumor mutation at baseline |  |  |
|-----------------------------------|--|--|--|--|
| Subject group type                | Subject analysis set                       | Subject analysis set                   |  |  |
| Number of subjects analysed       | 85   | 58                                     |  |  |
| Units: Percentage of participants |  |  |  |  |
| number (confidence interval 95%)  | 82.4 (72.57 to 89.77)                      | 69.0 (55.46 to 80.46)                  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: ORR in patient subgroups defined by molecular profile: Detectable in plasma derived ctDNA at baseline

|                 |   |
|-----------------|---|
| End point title | ORR in patient subgroups defined by molecular profile: Detectable in plasma derived ctDNA at baseline |
|-----------------|---|

End point description:

ORR is defined as the number (%) of patients with at least one visit response of complete response or partial response that is confirmed at least 4 weeks later. ORR was analysed in patient subgroups defined by molecular profile: Exon19del or L858R detectable in plasma derived ctDNA at baseline. The full analysis set included all patients who received at least 1 dose of Osimertinib.

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

End point timeframe:

From date of first dose until progression, or last evaluable assessment in the absence of progression, up to 5 years



| End point values                  | Exon19del-<br>Detectable in<br>plasma ctDNA<br>at baseline | L858R-<br>Detectable in<br>plasma ctDNA<br>at baseline |  |  |
|-----------------------------------|--|--|--|--|
| Subject group type                | Subject analysis set                                       | Subject analysis set                                   |  |  |
| Number of subjects analysed       | 62   | 46   |  |  |
| Units: Percentage of participants |  |  |  |  |
| number (confidence interval 95%)  | 85.5 (74.22 to 93.14)                                      | 71.7 (56.54 to 84.01)                                  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: TTD in patient subgroups defined by molecular profile: EGFR tumor mutation at baseline

|                 |  |
|-----------------|--|
| End point title | TTD in patient subgroups defined by molecular profile: EGFR tumor mutation at baseline |
|-----------------|--|

End point description:

TTD is defined as the time from the date of first dose of Osimertinib to the earliest of treatment discontinuation or death. TTD was analysed in patient subgroups defined by molecular profile: EGFR tumor mutation at baseline-Exon19del or L858R. The full analysis set included all patients who received at least 1 dose of Osimertinib.

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

End point timeframe:

From date of first dose to treatment discontinuation or death (by any cause in the absence of recurrence), up to 5 years

| End point values                 | Exon19del-<br>EGFR tumor<br>mutation at<br>baseline | L858R- EGFR<br>tumor mutation<br>at baseline |  |  |
|----------------------------------|---|--|--|--|
| Subject group type               | Subject analysis set                                | Subject analysis set                         |  |  |
| Number of subjects analysed      | 85  | 58   |  |  |
| Units: Months                    |   |  |  |  |
| median (confidence interval 95%) | 25.5 (19.6 to 32.1)                                 | 16.5 (12.1 to 21.7)                          |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: TTD in patient subgroups defined by molecular profile: Detectable in

## plasma derived ctDNA at baseline

|                 |   |
|-----------------|---|
| End point title | TTD in patient subgroups defined by molecular profile: Detectable in plasma derived ctDNA at baseline |
|-----------------|---|

### End point description:

TTD is defined as the time from the date of first dose of osimertinib to the earliest of treatment discontinuation or death. TTD was analysed in patient subgroups defined by molecular profile: Exon19del or L858R detectable in plasma derived ctDNA at baseline. The full analysis set included all patients who received at least one dose of Osimertinib.

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

### End point timeframe:

From date of first dose to treatment discontinuation or death (by any cause in the absence of recurrence), up to 5 years

| End point values                 | Exon19del-<br>Detectable in<br>plasma ctDNA<br>at baseline | L858R-<br>Detectable in<br>plasma ctDNA<br>at baseline |  |  |
|----------------------------------|--|--|--|--|
| Subject group type               | Subject analysis set                                       | Subject analysis set                                   |  |  |
| Number of subjects analysed      | 62   | 46   |  |  |
| Units: Months                    |  |  |  |  |
| median (confidence interval 95%) | 24.5 (17.8 to 29.6)  | 16.5 (12.1 to 21.4)                                    |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Tumour shrinkage/depth of response in patient subgroups defined by molecular profile: EGFR tumor mutation at baseline

|                 |   |
|-----------------|---|
| End point title | Tumour shrinkage/depth of response in patient subgroups defined by molecular profile: EGFR tumor mutation at baseline |
|-----------------|---|

### End point description:

Tumor shrinkage is defined as the best change from baseline in the sum of diameters of target lesions, in patient subgroups defined by molecular profile: EGFR tumor mutation at baseline-Exon19del or L858R. A negative change denotes a reduction in target lesion size. The full analysis set included all patients who received at least 1 dose of Osimertinib.

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

### End point timeframe:

From date of first dose until last recorded post baseline RECIST target lesion assessment scan, up to 5 years

| End point values            | Exon19del-<br>EGFR tumor<br>mutation at<br>baseline | L858R- EGFR<br>tumor mutation<br>at baseline |  |  |
|-----------------------------|---|--|--|--|
| Subject group type          | Subject analysis set                                | Subject analysis set                         |  |  |
| Number of subjects analysed | 83  | 55   |  |  |
| Units: Percentage change    |   |  |  |  |

|                               |                        |                        |  |  |
|-------------------------------|------------------------|------------------------|--|--|
| median (full range (min-max)) | -59.68 (-100.0 to 6.5) | -54.29 (-100.0 to 7.6) |  |  |
|-------------------------------|------------------------|------------------------|--|--|

## Statistical analyses

No statistical analyses for this end point

## Secondary: Tumour shrinkage/depth of response in patient subgroups defined by molecular profile: Detectable in plasma derived ctDNA at baseline

|                 |  |
|-----------------|--|
| End point title | Tumour shrinkage/depth of response in patient subgroups defined by molecular profile: Detectable in plasma derived ctDNA at baseline |
|-----------------|--|

End point description:

Tumour shrinkage is defined as the best change from baseline in the sum of diameters of target lesions, in patient subgroups defined by molecular profile: Exon19del or L858R detectable in plasma derived ctDNA at baseline. A negative change denotes a reduction in target lesion size. The full analysis set included all patients who received at least 1 dose of Osimertinib.

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

End point timeframe:

From date of first dose until last recorded post baseline RECIST target lesion assessment scan, up to 5 years

| End point values              | Exon19del-<br>Detectable in<br>plasma ctDNA<br>at baseline | L858R-<br>Detectable in<br>plasma ctDNA<br>at baseline |  |  |
|-------------------------------|--|--|--|--|
| Subject group type            | Subject analysis set                                       | Subject analysis set                                   |  |  |
| Number of subjects analysed   | 60   | 44   |  |  |
| Units: Percentage change      |  |  |  |  |
| median (full range (min-max)) | -60.80 (-100.0 to 6.5)                                     | -58.33 (-100.0 to 7.6)                                 |  |  |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From Day 1 to Follow-up (28 days post last dose) up to 5 years

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 26.1 |
|--------------------|------|

### Reporting groups

|                       |                   |
|-----------------------|-------------------|
| Reporting group title | Osimertinib 80 mg |
|-----------------------|-------------------|

Reporting group description:

Participants received Osimertinib 80mg orally once daily.

| Serious adverse events  | Osimertinib 80 mg |  |  |
|---|-------------------|--|--|
| Total subjects affected by serious adverse events                   |                   |  |  |
| subjects affected / exposed   | 53 / 154 (34.42%) |  |  |
| number of deaths (all causes)                                       | 40                |  |  |
| number of deaths resulting from adverse events                      | 12                |  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                   |  |  |
| Cervix carcinoma  |                   |  |  |
| subjects affected / exposed   | 1 / 154 (0.65%)   |  |  |
| occurrences causally related to treatment / all                     | 0 / 1             |  |  |
| deaths causally related to treatment / all                          | 0 / 0             |  |  |
| Vascular disorders  |                   |  |  |
| Embolism  |                   |  |  |
| subjects affected / exposed   | 1 / 154 (0.65%)   |  |  |
| occurrences causally related to treatment / all                     | 0 / 1             |  |  |
| deaths causally related to treatment / all                          | 0 / 0             |  |  |
| Deep vein thrombosis  |                   |  |  |
| subjects affected / exposed   | 1 / 154 (0.65%)   |  |  |
| occurrences causally related to treatment / all                     | 1 / 1             |  |  |
| deaths causally related to treatment / all                          | 0 / 0             |  |  |
| General disorders and administration site conditions                |                   |  |  |
| Asthenia  |                   |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 1 / 154 (0.65%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| General physical health deterioration           |                 |  |  |
| subjects affected / exposed                     | 1 / 154 (0.65%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Reproductive system and breast disorders        |                 |  |  |
| Vaginal haemorrhage                             |                 |  |  |
| subjects affected / exposed                     | 1 / 154 (0.65%) |  |  |
| occurrences causally related to treatment / all | 0 / 4           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Respiratory, thoracic and mediastinal disorders |                 |  |  |
| Haemoptysis                                     |                 |  |  |
| subjects affected / exposed                     | 1 / 154 (0.65%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Interstitial lung disease                       |                 |  |  |
| subjects affected / exposed                     | 2 / 154 (1.30%) |  |  |
| occurrences causally related to treatment / all | 2 / 2           |  |  |
| deaths causally related to treatment / all      | 1 / 1           |  |  |
| Dyspnoea  |                 |  |  |
| subjects affected / exposed                     | 2 / 154 (1.30%) |  |  |
| occurrences causally related to treatment / all | 0 / 2           |  |  |
| deaths causally related to treatment / all      | 0 / 1           |  |  |
| Asthma  |                 |  |  |
| subjects affected / exposed                     | 1 / 154 (0.65%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Respiratory failure                             |                 |  |  |
| subjects affected / exposed                     | 1 / 154 (0.65%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| Pneumothorax                                    |                 |  |  |
| subjects affected / exposed                     | 1 / 154 (0.65%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Pneumonitis                                     |                 |  |  |
| subjects affected / exposed                     | 2 / 154 (1.30%) |  |  |
| occurrences causally related to treatment / all | 2 / 2           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Pulmonary embolism                              |                 |  |  |
| subjects affected / exposed                     | 4 / 154 (2.60%) |  |  |
| occurrences causally related to treatment / all | 1 / 4           |  |  |
| deaths causally related to treatment / all      | 0 / 1           |  |  |
| Psychiatric disorders                           |                 |  |  |
| Mania   |                 |  |  |
| subjects affected / exposed                     | 1 / 154 (0.65%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Confusional state                               |                 |  |  |
| subjects affected / exposed                     | 1 / 154 (0.65%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Investigations                                  |                 |  |  |
| Platelet count decreased                        |                 |  |  |
| subjects affected / exposed                     | 1 / 154 (0.65%) |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Neutrophil count decreased                      |                 |  |  |
| subjects affected / exposed                     | 1 / 154 (0.65%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Electrocardiogram QT prolonged                  |                 |  |  |
| subjects affected / exposed                     | 1 / 154 (0.65%) |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| Injury, poisoning and procedural complications  |                 |  |  |
| Femoral neck fracture                           |                 |  |  |
| subjects affected / exposed                     | 1 / 154 (0.65%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Humerus fracture                                |                 |  |  |
| subjects affected / exposed                     | 1 / 154 (0.65%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Foreign body aspiration                         |                 |  |  |
| subjects affected / exposed                     | 1 / 154 (0.65%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Fibula fracture                                 |                 |  |  |
| subjects affected / exposed                     | 1 / 154 (0.65%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Pelvic fracture                                 |                 |  |  |
| subjects affected / exposed                     | 1 / 154 (0.65%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Wound dehiscence                                |                 |  |  |
| subjects affected / exposed                     | 1 / 154 (0.65%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Cardiac disorders                               |                 |  |  |
| Cardiac failure acute                           |                 |  |  |
| subjects affected / exposed                     | 1 / 154 (0.65%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 1           |  |  |
| Cardiac failure                                 |                 |  |  |
| subjects affected / exposed                     | 2 / 154 (1.30%) |  |  |
| occurrences causally related to treatment / all | 1 / 2           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| Atrial fibrillation                             |                 |  |  |
| subjects affected / exposed                     | 3 / 154 (1.95%) |  |  |
| occurrences causally related to treatment / all | 0 / 4           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Acute coronary syndrome                         |                 |  |  |
| subjects affected / exposed                     | 2 / 154 (1.30%) |  |  |
| occurrences causally related to treatment / all | 0 / 2           |  |  |
| deaths causally related to treatment / all      | 0 / 1           |  |  |
| Nervous system disorders                        |                 |  |  |
| Status epilepticus                              |                 |  |  |
| subjects affected / exposed                     | 1 / 154 (0.65%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Spinal cord compression                         |                 |  |  |
| subjects affected / exposed                     | 1 / 154 (0.65%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Peripheral sensory neuropathy                   |                 |  |  |
| subjects affected / exposed                     | 1 / 154 (0.65%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Blood and lymphatic system disorders            |                 |  |  |
| Immune thrombocytopenia                         |                 |  |  |
| subjects affected / exposed                     | 1 / 154 (0.65%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Blood loss anaemia                              |                 |  |  |
| subjects affected / exposed                     | 1 / 154 (0.65%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Anaemia   |                 |  |  |
| subjects affected / exposed                     | 1 / 154 (0.65%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |



|   |                 |  |  |
|---|-----------------|--|--|
| Gastrointestinal disorders                      |                 |  |  |
| Vomiting  |                 |  |  |
| subjects affected / exposed                     | 1 / 154 (0.65%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 1           |  |  |
| Gastritis                                       |                 |  |  |
| subjects affected / exposed                     | 3 / 154 (1.95%) |  |  |
| occurrences causally related to treatment / all | 0 / 3           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Duodenitis                                      |                 |  |  |
| subjects affected / exposed                     | 1 / 154 (0.65%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Hepatobiliary disorders                         |                 |  |  |
| Cholecystitis                                   |                 |  |  |
| subjects affected / exposed                     | 1 / 154 (0.65%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Skin and subcutaneous tissue disorders          |                 |  |  |
| Subcutaneous emphysema                          |                 |  |  |
| subjects affected / exposed                     | 1 / 154 (0.65%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Renal and urinary disorders                     |                 |  |  |
| Acute kidney injury                             |                 |  |  |
| subjects affected / exposed                     | 2 / 154 (1.30%) |  |  |
| occurrences causally related to treatment / all | 0 / 2           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Haematuria                                      |                 |  |  |
| subjects affected / exposed                     | 1 / 154 (0.65%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Renal impairment                                |                 |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 1 / 154 (0.65%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Endocrine disorders                             |                 |  |  |
| Adrenal insufficiency                           |                 |  |  |
| subjects affected / exposed                     | 1 / 154 (0.65%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Musculoskeletal and connective tissue disorders |                 |  |  |
| Back pain                                       |                 |  |  |
| subjects affected / exposed                     | 1 / 154 (0.65%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Infections and infestations                     |                 |  |  |
| COVID-19  |                 |  |  |
| subjects affected / exposed                     | 1 / 154 (0.65%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Urosepsis                                       |                 |  |  |
| subjects affected / exposed                     | 1 / 154 (0.65%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Urinary tract infection                         |                 |  |  |
| subjects affected / exposed                     | 3 / 154 (1.95%) |  |  |
| occurrences causally related to treatment / all | 0 / 3           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Tuberculosis                                    |                 |  |  |
| subjects affected / exposed                     | 1 / 154 (0.65%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Sepsis  |                 |  |  |
| subjects affected / exposed                     | 4 / 154 (2.60%) |  |  |
| occurrences causally related to treatment / all | 0 / 4           |  |  |
| deaths causally related to treatment / all      | 0 / 2           |  |  |

|   |                  |  |  |
|---|------------------|--|--|
| Respiratory tract infection                     |                  |  |  |
| subjects affected / exposed                     | 1 / 154 (0.65%)  |  |  |
| occurrences causally related to treatment / all | 0 / 1            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Pneumonia aspiration                            |                  |  |  |
| subjects affected / exposed                     | 1 / 154 (0.65%)  |  |  |
| occurrences causally related to treatment / all | 0 / 1            |  |  |
| deaths causally related to treatment / all      | 0 / 1            |  |  |
| Pneumonia                                       |                  |  |  |
| subjects affected / exposed                     | 12 / 154 (7.79%) |  |  |
| occurrences causally related to treatment / all | 0 / 12           |  |  |
| deaths causally related to treatment / all      | 0 / 3            |  |  |
| Lower respiratory tract infection               |                  |  |  |
| subjects affected / exposed                     | 1 / 154 (0.65%)  |  |  |
| occurrences causally related to treatment / all | 0 / 1            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Gastroenteritis                                 |                  |  |  |
| subjects affected / exposed                     | 2 / 154 (1.30%)  |  |  |
| occurrences causally related to treatment / all | 0 / 2            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Metabolism and nutrition disorders              |                  |  |  |
| Hyperglycaemic hyperosmolar nonketotic syndrome |                  |  |  |
| subjects affected / exposed                     | 1 / 154 (0.65%)  |  |  |
| occurrences causally related to treatment / all | 0 / 1            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Hyponatraemia                                   |                  |  |  |
| subjects affected / exposed                     | 2 / 154 (1.30%)  |  |  |
| occurrences causally related to treatment / all | 0 / 2            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |
| Hypokalaemia                                    |                  |  |  |
| subjects affected / exposed                     | 1 / 154 (0.65%)  |  |  |
| occurrences causally related to treatment / all | 0 / 1            |  |  |
| deaths causally related to treatment / all      | 0 / 0            |  |  |

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

| <b>Non-serious adverse events</b>                     | Osimertinib 80 mg  |  |  |
|---|--------------------|--|--|
| Total subjects affected by non-serious adverse events |                    |  |  |
| subjects affected / exposed                           | 148 / 154 (96.10%) |  |  |
| Investigations  |                    |  |  |
| Gamma-glutamyltransferase increased                   |                    |  |  |
| subjects affected / exposed                           | 9 / 154 (5.84%)    |  |  |
| occurrences (all)                                     | 16                 |  |  |
| Platelet count decreased                              |                    |  |  |
| subjects affected / exposed                           | 11 / 154 (7.14%)   |  |  |
| occurrences (all)                                     | 16                 |  |  |
| Weight decreased                                      |                    |  |  |
| subjects affected / exposed                           | 11 / 154 (7.14%)   |  |  |
| occurrences (all)                                     | 14                 |  |  |
| Aspartate aminotransferase increased                  |                    |  |  |
| subjects affected / exposed                           | 14 / 154 (9.09%)   |  |  |
| occurrences (all)                                     | 14                 |  |  |
| Alanine aminotransferase increased                    |                    |  |  |
| subjects affected / exposed                           | 16 / 154 (10.39%)  |  |  |
| occurrences (all)                                     | 16                 |  |  |
| Nervous system disorders                              |                    |  |  |
| Headache  |                    |  |  |
| subjects affected / exposed                           | 11 / 154 (7.14%)   |  |  |
| occurrences (all)                                     | 11                 |  |  |
| Dizziness   |                    |  |  |
| subjects affected / exposed                           | 11 / 154 (7.14%)   |  |  |
| occurrences (all)                                     | 12                 |  |  |
| Blood and lymphatic system disorders                  |                    |  |  |
| Anaemia   |                    |  |  |
| subjects affected / exposed                           | 26 / 154 (16.88%)  |  |  |
| occurrences (all)                                     | 34                 |  |  |

|  |   |  |  |
|--|---|--|--|
| Thrombocytopenia<br>subjects affected / exposed<br>occurrences (all)   | 9 / 154 (5.84%)<br>10   |  |  |
| General disorders and administration<br>site conditions<br>Fatigue<br>subjects affected / exposed<br>occurrences (all)<br><br>Asthenia<br>subjects affected / exposed<br>occurrences (all)   | 11 / 154 (7.14%)<br>17<br><br>13 / 154 (8.44%)<br>14  |  |  |
| Gastrointestinal disorders<br>Constipation<br>subjects affected / exposed<br>occurrences (all)<br><br>Gastritis<br>subjects affected / exposed<br>occurrences (all)<br><br>Diarrhoea<br>subjects affected / exposed<br>occurrences (all)<br><br>Vomiting<br>subjects affected / exposed<br>occurrences (all)<br><br>Stomatitis<br>subjects affected / exposed<br>occurrences (all)<br><br>Mouth ulceration<br>subjects affected / exposed<br>occurrences (all)<br><br>Nausea<br>subjects affected / exposed<br>occurrences (all) | 13 / 154 (8.44%)<br>16<br><br>8 / 154 (5.19%)<br>9<br><br>63 / 154 (40.91%)<br>94<br><br>14 / 154 (9.09%)<br>16<br><br>22 / 154 (14.29%)<br>30<br><br>15 / 154 (9.74%)<br>20<br><br>17 / 154 (11.04%)<br>21 |  |  |
| Respiratory, thoracic and mediastinal<br>disorders<br>Dyspnoea<br>subjects affected / exposed<br>occurrences (all)   | 8 / 154 (5.19%)<br>10   |  |  |

|  |                         |  |  |
|--|-------------------------|--|--|
| Cough<br>subjects affected / exposed<br>occurrences (all)                | 32 / 154 (20.78%)<br>36 |  |  |
| Productive cough<br>subjects affected / exposed<br>occurrences (all)     | 9 / 154 (5.84%)<br>9    |  |  |
| Skin and subcutaneous tissue disorders                                   |                         |  |  |
| Rash<br>subjects affected / exposed<br>occurrences (all)                 | 26 / 154 (16.88%)<br>30 |  |  |
| Pruritus<br>subjects affected / exposed<br>occurrences (all)             | 23 / 154 (14.94%)<br>27 |  |  |
| Dry skin<br>subjects affected / exposed<br>occurrences (all)             | 30 / 154 (19.48%)<br>37 |  |  |
| Dermatitis acneiform<br>subjects affected / exposed<br>occurrences (all) | 21 / 154 (13.64%)<br>32 |  |  |
| Psychiatric disorders  |                         |  |  |
| Insomnia<br>subjects affected / exposed<br>occurrences (all)             | 10 / 154 (6.49%)<br>11  |  |  |
| Musculoskeletal and connective tissue disorders                          |                         |  |  |
| Pain in extremity<br>subjects affected / exposed<br>occurrences (all)    | 10 / 154 (6.49%)<br>12  |  |  |
| Back pain<br>subjects affected / exposed<br>occurrences (all)            | 18 / 154 (11.69%)<br>21 |  |  |
| Arthralgia<br>subjects affected / exposed<br>occurrences (all)           | 16 / 154 (10.39%)<br>20 |  |  |
| Infections and infestations  |                         |  |  |
| Upper respiratory tract infection  |                         |  |  |

|                                    |                   |  |  |
|------------------------------------|-------------------|--|--|
| subjects affected / exposed        | 24 / 154 (15.58%) |  |  |
| occurrences (all)                  | 39                |  |  |
| Urinary tract infection            |                   |  |  |
| subjects affected / exposed        | 16 / 154 (10.39%) |  |  |
| occurrences (all)                  | 21                |  |  |
| COVID-19                           |                   |  |  |
| subjects affected / exposed        | 14 / 154 (9.09%)  |  |  |
| occurrences (all)                  | 14                |  |  |
| Paronychia                         |                   |  |  |
| subjects affected / exposed        | 36 / 154 (23.38%) |  |  |
| occurrences (all)                  | 72                |  |  |
| Metabolism and nutrition disorders |                   |  |  |
| Decreased appetite                 |                   |  |  |
| subjects affected / exposed        | 27 / 154 (17.53%) |  |  |
| occurrences (all)                  | 32                |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date          | Amendment  |
|---------------|--|
| 14 April 2023 | There had been substantial amendment of the Protocol Version 2.0 on 05Sep17, version 3.0 on 24 January 2018, Version 4.0 on 25 September 2018, Version 5.0, 28 April 2022, Version 6.0, 02 November 2022 and Version 7.0 14 April 2023 |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported