Clinical trial results:
A Phase III, Double-blind, Randomised Study to Assess the Efficacy and Safety of AZD9291 versus a Standard of Care Epidermal Growth Factor Receptor-Tyrosine Kinase Inhibitor as First-line Treatment in Patients with Epidermal Growth Factor Receptor Mutation-positive, Locally-advanced or Metastatic Non-small-cell Lung Cancer (FLAURA)

Summary

EudraCT number	2014-002694-11
Trial protocol	HU GB IT DE ES BE SE CZ FR PL BG PT
Global end of trial date	20 November 2025

Results information

Result version number	v1 (current)
This version publication date	01 April 2026
First version publication date	01 April 2026

Trial information

Trial identification

Sponsor protocol code	D5160C00007

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02296125
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca AB
Sponsor organisation address	Not applicable, Södertälje, Sweden, SE-151 85
Public contact	Global Clinical Lead, AstraZeneca AB, 1 +46 766 346712, ClinicalTrialTransparency@astrazeneca.com
Scientific contact	Global Clinical Leader, AstraZeneca AB, 1 +46 766 346712, ClinicalTrialTransparency@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	25 June 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 November 2025
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of single agent osimertinib compared with SoC EGFR-TKI therapy as measured by progression free survival (PFS).

Protection of trial subjects:

This study was performed in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with International Conference on Harmonisation (ICH)/Good Clinical Practice (GCP), applicable regulatory requirements, and the AstraZeneca policy on Bioethics. The study was approved by the institutional review board (IRB)/independent ethics committee (IEC) associated with each study centre. All CSP amendments were approved by each IRB/IEC and, if applicable, the national regulatory authority before implementation. Local requirements were followed for the revised CSPs. If a CSP amendment required a change to a study centre's informed consent form (ICF), AstraZeneca and the study centre's IRB/IEC approved the revised ICF before the revised ICF was used. Informed consent was obtained from all patients prior to enrolment into the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 December 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 25
Country: Number of subjects enrolled	Belgium: 12
Country: Number of subjects enrolled	Brazil: 1
Country: Number of subjects enrolled	Canada: 18
Country: Number of subjects enrolled	China: 136
Country: Number of subjects enrolled	Czechia: 2
Country: Number of subjects enrolled	France: 13
Country: Number of subjects enrolled	Germany: 16
Country: Number of subjects enrolled	Hungary: 5
Country: Number of subjects enrolled	Israel: 8
Country: Number of subjects enrolled	Italy: 21
Country: Number of subjects enrolled	Japan: 121
Country: Number of subjects enrolled	Malaysia: 22
Country: Number of subjects enrolled	Philippines: 9
Country: Number of subjects enrolled	Poland: 8
Country: Number of subjects enrolled	Portugal: 7

Country: Number of subjects enrolled	Romania: 2
Country: Number of subjects enrolled	Russian Federation: 18
Country: Number of subjects enrolled	Korea, Republic of: 47
Country: Number of subjects enrolled	Spain: 27
Country: Number of subjects enrolled	Sweden: 2
Country: Number of subjects enrolled	Switzerland: 6
Country: Number of subjects enrolled	Taiwan: 24
Country: Number of subjects enrolled	Thailand: 74
Country: Number of subjects enrolled	Turkey: 1
Country: Number of subjects enrolled	Ukraine: 8
Country: Number of subjects enrolled	United Kingdom: 11
Country: Number of subjects enrolled	United States: 23
Country: Number of subjects enrolled	Viet Nam: 6
Worldwide total number of subjects	673
EEA total number of subjects	115

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)	372
From 65 to 84 years	295
85 years and over	6

Subject disposition

Recruitment

Recruitment details:

A total of 556 subjects in Global cohort were randomized to treatment in 29 countries. Further 117 subjects enrolled into China cohort. There were 19 Chinese subjects who were included in both global and China cohorts giving total of 692. To avoid tool error 19 subjects have been double counted for Country China under-Population of Trial Subjects.

Pre-assignment

Screening details:

Subjects were enrolled based on presence in their tumour of at least 1 of 2 most frequent Epidermal growth factor receptor (EGFR) mutations. At time of enrolment, all subjects were required to provide biopsy tissue for central testing of Exon 19 deletion (Ex19del) and L858R mutations. Subjects were treatment-naïve for their advanced EGFRm NSCLC.

Period 1

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

Arms

Are arms mutually exclusive?	No
Arm title	Osimertinib 80 mg (Global Cohort)

Arm description:

Randomized subjects received Osimertinib 80 mg orally once daily (QD)

Arm type	Experimental
Investigational medicinal product name	Osimertinib
Investigational medicinal product code	AZD9291
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received once-daily oral administration of Osimertinib (80 mg and 40 mg tablets)

Arm title	SoC EGFR-TKI (Global Cohort)

Arm description:

Randomized subjects received Standard of care (SoC) Epidermal growth factor receptor-tyrosine kinase inhibitor (EGFR-TKI). Participants received gefitinib 250 mg orally QD or erlotinib 150 mg orally QD

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

Dosage and administration details:

Subjects received erlotinib 150 mg orally once daily

Investigational medicinal product name	Gefitinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received gefitinib 250 mg orally once daily

Arm title	Osimertinib 80 mg (China Cohort)

Arm description:

Randomized subjects received Osimertinib 80 mg orally once daily (QD)

Arm type	Experimental
Investigational medicinal product name	Osimertinib
Investigational medicinal product code	AZD9291
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received once-daily oral administration of Osimertinib (80 mg and 40 mg tablets)

Arm title	SoC EGFR-TKI (China Cohort)

Arm description:

Randomized subjects received Standard of care (SoC) Epidermal growth factor receptor-tyrosine kinase inhibitor (EGFRTKI). Participants received gefitinib 250 mg orally QD

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

Dosage and administration details:

Subjects received gefitinib 250 mg orally once daily

Number of subjects in period 1	Osimertinib 80 mg (Global Cohort)	SoC EGFR-TKI (Global Cohort)	Osimertinib 80 mg (China Cohort)
Started	279	277	71
Completed	61	13	15
Not completed	218	264	56
Severe non-compliance to protocol	-	1	-
Consent withdrawn by subject	18	8	6
Adverse event, non-fatal	41	52	9
Any reason not specifically recorded	6	4	2
Condition under investigation worsened	153	199	39

Number of subjects in period 1	SoC EGFR-TKI (China Cohort)
Started	65
Completed	3
Not completed	62
Severe non-compliance to protocol	-

Consent withdrawn by subject	2
Adverse event, non-fatal	4
Any reason not specifically recorded	-
Condition under investigation worsened	56

Baseline characteristics

Reporting groups	
Reporting group title	Osimertinib 80 mg (Global Cohort)
Reporting group description:	
Randomized subjects received Osimertinib 80 mg orally once daily (QD)	
Reporting group title	SoC EGFR-TKI (Global Cohort)
Reporting group description:	
Randomized subjects received Standard of care (SoC) Epidermal growth factor receptor-tyrosine kinase inhibitor (EGFR-TKI). Participants received gefitinib 250 mg orally QD or erlotinib 150 mg orally QD	
Reporting group title	Osimertinib 80 mg (China Cohort)
Reporting group description:	
Randomized subjects received Osimertinib 80 mg orally once daily (QD)	
Reporting group title	SoC EGFR-TKI (China Cohort)
Reporting group description:	
Randomized subjects received Standard of care (SoC) Epidermal growth factor receptor-tyrosine kinase inhibitor (EGFRTKI). Participants received gefitinib 250 mg orally QD	

Reporting group values	Osimertinib 80 mg (Global Cohort)	SoC EGFR-TKI (Global Cohort)	Osimertinib 80 mg (China Cohort)
Number of subjects	279	277	71
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)	153	145	49
From 65-84 years	125	127	22
85 years and over	1	5	0
Age Continuous			
Units: years			
arithmetic mean	62.7	63.3	59.1
standard deviation	± 10.70	± 10.90	± 9.66
Sex: Female, Male			
Units: Participants			
Female	178	172	43
Male	101	105	28
Smoking status			
Units: Subjects			
Never smoked	182	175	53
Current smokers	8	9	3
Former smokers	89	93	15

Reporting group values	SoC EGFR-TKI (China Cohort)	Total	
Number of subjects	65	692	

Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	42	389	
From 65-84 years	23	297	
85 years and over	0	6	
Age Continuous Units: years			
arithmetic mean	59.0		
standard deviation	± 10.94	-	
Sex: Female, Male Units: Participants			
Female	46	439	
Male	19	253	
Smoking status Units: Subjects			
Never smoked	50	460	
Current smokers	4	24	
Former smokers	11	208	

End points

End points reporting groups	
Reporting group title	Osimertinib 80 mg (Global Cohort)
Reporting group description:	
Randomized subjects received Osimertinib 80 mg orally once daily (QD)	
Reporting group title	SoC EGFR-TKI (Global Cohort)
Reporting group description:	
Randomized subjects received Standard of care (SoC) Epidermal growth factor receptor-tyrosine kinase inhibitor (EGFR-TKI). Participants received gefitinib 250 mg orally QD or erlotinib 150 mg orally QD	
Reporting group title	Osimertinib 80 mg (China Cohort)
Reporting group description:	
Randomized subjects received Osimertinib 80 mg orally once daily (QD)	
Reporting group title	SoC EGFR-TKI (China Cohort)
Reporting group description:	
Randomized subjects received Standard of care (SoC) Epidermal growth factor receptor-tyrosine kinase inhibitor (EGFRTKI). Participants received gefitinib 250 mg orally QD	

Primary: Median progression free survival (PFS) (months)	
End point title	Median progression free survival (PFS) (months)
End point description:	
Progression-free survival was defined as the time from randomization until the date of objective disease progression or death (by any cause in the absence of progression) regardless of whether the participant withdrew from randomized therapy or received another anti-cancer therapy prior to progression and was used to assess the efficacy of single agent osimertinib compared with SoC EGFR-TKI therapy as measured by PFS. The primary endpoint of PFS was based on based on Investigator assessment according to Response Evaluation Criteria in Solid Tumors version (RECIST v1.1).	
End point type	Primary
End point timeframe:	
At baseline and every 6 weeks for the first 18 months and then every 12 weeks relative to randomisation until progression	

End point values	Osimertinib 80 mg (Global Cohort)	SoC EGFR-TKI (Global Cohort)	Osimertinib 80 mg (China Cohort)	SoC EGFR-TKI (China Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	279	277	71	65
Units: Months				
median (confidence interval 95%)	18.9 (15.2 to 21.4)	10.2 (9.6 to 11.1)	17.8 (13.6 to 20.7)	9.8 (8.3 to 13.8)

Statistical analyses

Statistical analysis title	Osimertinib 80 mg vs SoC EGFR-TKI (Global Cohort)
Comparison groups	Osimertinib 80 mg (Global Cohort) v SoC EGFR-TKI (Global Cohort)

Number of subjects included in analysis	556
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.37
upper limit	0.57

Statistical analysis title	Osimertinib 80 mg vs SoC EGFR-TKI (China Cohort)
Comparison groups	Osimertinib 80 mg (China Cohort) v SoC EGFR-TKI (China Cohort)
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0065
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.37
upper limit	0.85

Primary: Percentage of subjects in progression free survival at 6, 12, and 18 months

End point title	Percentage of subjects in progression free survival at 6, 12, and 18 months[1]

End point description:

Progression-free survival was defined as the time from randomization until the date of objective disease progression or death (by any cause in the absence of progression) regardless of whether the subject withdrew from randomized therapy or received another anti-cancer therapy prior to progression and was used to assess the efficacy of single agent osimertinib compared with SoC EGFR-TKI therapy as measured by PFS.

End point type	Primary

End point timeframe:

At baseline and every 6 weeks for the first 18 months and then every 12 weeks relative to randomisation until progression

Notes:

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

End point values	Osimertinib 80 mg (Global Cohort)	SoC EGFR-TKI (Global Cohort)	Osimertinib 80 mg (China Cohort)	SoC EGFR-TKI (China Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	279	277	71	65
Units: Percentage of Subjects				
number (not applicable)				
Progression free at 6 months (%)	88.4	75.2	78.8	72.3
Progression free at 12 months (%)	68.2	42.3	67.3	44.6
Progression free at 18 months (%)	50.9	24.4	46.9	25.8

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 was defined as the number (%) of subjects with measurable disease with at least 1 visit response of Complete response (CR) or Partial response (PR) and it was used to further assess the efficacy of osimertinib compared with SoC EGFR-TKI therapy. ORR was based on Investigator assessment according to RECIST v1.1.

End point type	Secondary

End point timeframe:

At baseline and every 6 weeks for the first 18 months and then every 12 weeks relative to randomisation until progression

End point values	Osimertinib 80 mg (Global Cohort)	SoC EGFR-TKI (Global Cohort)	Osimertinib 80 mg (China Cohort)	SoC EGFR-TKI (China Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	279	277	71	65
Units: Percentage of subjects				
number (confidence interval 95%)	76.7 (71.29 to 81.53)	69.0 (63.14 to 74.35)	76.1 (64.5 to 85.4)	70.8 (58.2 to 81.4)

Statistical analyses

Statistical analysis title	Osimertinib 80 mg vs SoC EGFR-TKI (Global Cohort)
Comparison groups	Osimertinib 80 mg (Global Cohort) v SoC EGFR-TKI (Global Cohort)

Number of subjects included in analysis	556
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.036
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.03
upper limit	2.22

Statistical analysis title	Osimertinib 80 mg vs SoC EGFR-TKI (China Cohort)
Comparison groups	Osimertinib 80 mg (China Cohort) v SoC EGFR-TKI (China Cohort)
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.485
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.61
upper limit	2.84

Secondary: Duration of response (DoR)

End point title	Duration of response (DoR)

End point description:

Duration of response was defined as the time from the date of first documented response until the date of documented progression or death in the absence of disease progression and was used to further assess the efficacy of osimertinib compared with SoC EGFR-TKI therapy. Here arbitrary number 999.999 reflects that upper limit is not calculable at this data cut-off.

End point type	Secondary

End point timeframe:

At baseline and every 6 weeks for the first 18 months and then every 12 weeks until objective disease progression

End point values	Osimertinib 80 mg (Global Cohort)	SoC EGFR-TKI (Global Cohort)	Osimertinib 80 mg (China Cohort)	SoC EGFR-TKI (China Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	279	277	71	65
Units: Months				
median (confidence interval 95%)	17.2 (13.8 to 22.0)	8.5 (7.3 to 9.8)	16.4 (12.3 to 999.999)	10.9 (8.3 to 13.8)

Statistical analyses

Statistical analysis title	Osimertinib 80 mg vs SoC EGFR-TKI (China Cohort)
Comparison groups	Osimertinib 80 mg (China Cohort) v SoC EGFR-TKI (China Cohort)
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0133
Method	Log Normal Distribution
Parameter estimate	Mean difference (final values)
Point estimate	2.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.21
upper limit	5.09

Statistical analysis title	Osimertinib 80 mg vs SoC EGFR-TKI (Global Cohort)
Comparison groups	Osimertinib 80 mg (Global Cohort) v SoC EGFR-TKI (Global Cohort)
Number of subjects included in analysis	556
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.0001
Method	Log Normal Distribution
Parameter estimate	Mean difference (final values)
Point estimate	2.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.68
upper limit	3.08

Secondary: Disease control rate (DCR)

End point title	Disease control rate (DCR)

End point description:

The DCR was defined as the percentage of subjects who had a best overall response (BOR) of Complete response (CR), Partial response (PR) or Stable disease (SD) ≥6 weeks prior to any Progressive disease (PD) event and was used to further assess the efficacy of osimertinib compared with SoC EGFR-TKI therapy. DCR was based on Investigator assessment according to RECIST v1.1.

End point type	Secondary

End point timeframe:

At baseline and every 6 weeks for the first 18 months and then every 12 weeks until objective disease progression

End point values	Osimertinib 80 mg (Global Cohort)	SoC EGFR-TKI (Global Cohort)	Osimertinib 80 mg (China Cohort)	SoC EGFR-TKI (China Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	279	277	71	65
Units: Percentage of Subjects				
number (confidence interval 95%)	97.1 (94.4 to 98.8)	92.4 (88.6 to 95.2)	97.2 (90.2 to 99.7)	95.4 (87.1 to 99.0)

Statistical analyses

Statistical analysis title	Osimertinib 80 mg vs SoC EGFR-TKI (Global Cohort)
Comparison groups	Osimertinib 80 mg (Global Cohort) v SoC EGFR-TKI (Global Cohort)
Number of subjects included in analysis	556
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.011
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.25
upper limit	6.78

Statistical analysis title	Osimertinib 80 mg vs SoC EGFR-TKI (China Cohort)
Comparison groups	Osimertinib 80 mg (China Cohort) v SoC EGFR-TKI (China Cohort)
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.5772
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.67

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.27
upper limit	12.98

Secondary: Depth of response

End point title	Depth of response

End point description:

The Depth of response was defined as the relative change in the sum of the longest diameters of Response Evaluation Criteria in Solid Tumors (RECIST) Target lesions (TLs) at the nadir, in the absence of new lesions (NLs) or progression of Non-target lesions (NTLs), compared to baseline and was used to further assess the efficacy of osimertinib compared with SoC EGFR-TKI therapy

End point type	Secondary

End point timeframe:

At baseline and every 6 weeks for the first 18 months and then every 12 weeks until objective disease progression

End point values	Osimertinib 80 mg (Global Cohort)	SoC EGFR-TKI (Global Cohort)	Osimertinib 80 mg (China Cohort)	SoC EGFR-TKI (China Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	279	277	71	65
Units: Percentage of Change				
arithmetic mean (standard deviation)	-52.36 (± 25.065)	-45.66 (± 28.270)	-49.17 (± 24.303)	-42.92 (± 26.814)

Statistical analyses

Statistical analysis title	Osimertinib 80 mg vs SoC EGFR-TKI (China Cohort)
Comparison groups	Osimertinib 80 mg (China Cohort) v SoC EGFR-TKI (China Cohort)
Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1348
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-6.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.246
upper limit	2.072

Statistical analysis title	Osimertinib 80 mg vs SoC EGFR-TKI (Global Cohort)
Comparison groups	Osimertinib 80 mg (Global Cohort) v SoC EGFR-TKI (Global Cohort)
Number of subjects included in analysis	556
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0025
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-6.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.205
upper limit	-2.403

Secondary: Overall Survival (OS)- Number of Subjects with an Event	
End point title	Overall Survival (OS)- Number of Subjects with an Event
End point description:	
Overall survival was defined as the time from the date of randomisation until death from any cause and was used to further assess the efficacy of osimertinib compared with SoC EGFR-TKI therapy	
End point type	Secondary
End point timeframe:	
From first dose to end of study or date of death from any cause, whichever comes first, assessed every 6 weeks (approximately 29 months)	

End point values	Osimertinib 80 mg (Global Cohort)	SoC EGFR-TKI (Global Cohort)	Osimertinib 80 mg (China Cohort)	SoC EGFR-TKI (China Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	279	277	71	65
Units: Subjects				
Death	155	166	45	44
Still in survival follow-up	104	86	25	17
Terminated prior to death	20	25	1	4

Statistical analyses

Statistical analysis title	Osimertinib 80 mg vs SoC EGFR-TKI (China Cohort)
Comparison groups	Osimertinib 80 mg (China Cohort) v SoC EGFR-TKI (China Cohort)

Number of subjects included in analysis	136
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.4416
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.848
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5568
upper limit	1.291

Statistical analysis title	Osimertinib 80 mg vs SoC EGFR-TKI (Global Cohort)
Comparison groups	Osimertinib 80 mg (Global Cohort) v SoC EGFR-TKI (Global Cohort)
Number of subjects included in analysis	556
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.0462
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.799
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6409
upper limit	0.9963

Secondary: Plasma concentrations of AZD9291

End point title	Plasma concentrations of AZD9291[2]

End point description:

To characterise the pharmacokinetics (PK) of osimertinib. Here arbitrary number "9999.9999" reflects that the values were non-quantifiable and not calculable.

End point type	Secondary

End point timeframe:

Blood samples collected from each participant at pre-dose, 0.5 to 2 hours, and 3 to 5 hours post-dose on Day 1 Cycle 1, and every other cycle thereafter up to and including Cycle 13 (approximately 9 months)

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analyses have been performed

End point values	Osimertinib 80 mg (Global Cohort)	Osimertinib 80 mg (China Cohort)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	279	71		
Units: Nano moles				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1-Predose	9999.9999 (± 9999.9999)	9999.9999 (± 9999.9999)		
Cycle 1 Day 1-0.5 - 2 hours	4.9487 (± 1173.3679)	5.0249 (± 816.7305)		
Cycle 1 Day 1-3 - 5 hours	129.3340 (± 171.2983)	131.5669 (± 120.5979)		
Cycle 3 Day 1- Predose	394.3489 (± 43.9296)	441.5606 (± 55.0039)		
Cycle 3 Day 1, 0.5 - 2 hours	397.7406 (± 45.8548)	441.7343 (± 60.0626)		
Cycle 3 Day 1, 3 - 5 hours	512.4012 (± 44.0653)	553.8090 (± 60.9883)		
Cycle 5 Day 1, Predose	358.5487 (± 53.8212)	419.5893 (± 63.2507)		
Cycle 5 Day 1, 0.5 - 2 hours	369.0696 (± 51.3284)	426.8197 (± 60.3841)		
Cycle 5 Day 1, 3-5 hours	485.8142 (± 47.2759)	570.7729 (± 61.4401)		
Cycle 7 Day 1-Predose	347.6176 (± 47.7442)	397.5857 (± 54.9006)		
Cycle 7 Day 1-0.5 - 2 hours	357.8529 (± 45.0713)	411.6170 (± 49.4107)		
Cycle 7 Day 1-3-5 hours	475.6587 (± 41.5778)	530.7212 (± 56.5184)		
Cycle 9 Day 1-Predose	359.5284 (± 47.0592)	383.2238 (± 67.7153)		
Cycle 9 Day 1-0.5-2 hours	363.0106 (± 48.3837)	395.2179 (± 71.5532)		
Cycle 9 Day 1-3-5 hours	485.6006 (± 46.6459)	490.5964 (± 70.3383)		
Cycle 11 Day 1-Predose	354.5330 (± 44.4308)	410.4023 (± 66.2329)		
Cycle 11 Day 1-0.5 -2 hours	367.7450 (± 45.2003)	415.2427 (± 64.6174)		
Cycle 11 Day 1-3-5 hours	476.4472 (± 44.4457)	528.8081 (± 68.4645)		
Cycle 13 Day 1-Predose	369.9834 (± 40.1071)	404.2678 (± 62.0291)		
Cycle 13 Day 1-0.5 -2 hours	371.4157 (± 42.9794)	393.1688 (± 62.1053)		
Cycle 13 Day 1-3-5 hours	496.6866 (± 40.8757)	499.0220 (± 62.5485)		

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma concentrations of metabolites AZ5104

End point title	Plasma concentrations of metabolites AZ5104[3]

End point description:

To characterise the pharmacokinetics (PK) of osimertinib metabolite AZ5104. Here arbitrary number "9999.9999" reflects that the values were non-quantifiable and not calculable.

End point type	Secondary

End point timeframe:

Blood samples collected from each participant at pre-dose, 0.5 to 2 hours, and 3 to 5 hours post-dose on Day 1 Cycle 1, and every other cycle thereafter up to and including Cycle 13 (approximately 9 months)

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analyses have been performed

End point values	Osimertinib 80 mg (Global Cohort)	Osimertinib 80 mg (China Cohort)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	279	71		
Units: Nano moles				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1 Predose	9999.9999 (± 9999.9999)	9999.9999 (± 9999.9999)		
Cycle 1 Day 1-0.5 - 2 hours	0.1542 (± 230.5161)	9999.9999 (± 9999.9999)		
Cycle 1 Day 1-3 - 5 hours	3.9399 (± 153.7651)	6.3053 (± 123.9308)		
Cycle 3 Day 1-Predose	42.9123 (± 50.2410)	56.8319 (± 51.0378)		
Cycle 3 Day 1, 0.5 - 2 hours	42.7434 (± 52.8557)	55.9947 (± 59.1318)		
Cycle 3 Day 1, 3 - 5 hours	48.3547 (± 50.4286)	64.0621 (± 54.2058)		
Cycle 5 Day 1, Predose	39.3718 (± 56.6226)	56.0330 (± 57.5022)		
Cycle 5 Day 1, 0.5 - 2 hours	39.4145 (± 55.3468)	55.3767 (± 55.9096)		
Cycle 5 Day 1, 3-5 hours	45.6842 (± 54.3876)	63.9216 (± 56.4249)		
Cycle 7 Day 1- Predose	38.3847 (± 50.0861)	52.5786 (± 51.0588)		
Cycle 7 Day 1, 0.5-2 hours	38.5301 (± 49.6296)	52.7638 (± 47.4797)		
Cycle 7 Day 1, 3-5 hours	44.4670 (± 48.4730)	60.6201 (± 50.6931)		
Cycle 9 Day 1, Predose	40.1230 (± 47.0682)	54.4349 (± 51.3447)		
Cycle 9 Day 1, 0.5-2 hours	40.4987 (± 47.6483)	54.7158 (± 54.6783)		
Cycle 9 Day 1, 3-5 hours	46.0310 (± 44.6875)	60.4649 (± 52.6147)		
Cycle 11 Day 1, Predose	38.3859 (± 48.5351)	56.4782 (± 59.1303)		
Cycle 11 Day 1, 0.5-2 hours	38.7620 (± 48.1414)	57.4095 (± 57.0891)		
Cycle 11 Day 1, 3-5 hours	43.9135 (± 50.6779)	65.1943 (± 58.5043)		
Cycle 13 Day 1, Predose	40.4356 (± 47.2671)	55.1162 (± 54.3493)		

Cycle 13 Day 1, 0.5- 2 hours	40.1116 (± 46.3929)	54.3858 (± 49.9148)		
Cycle 13 Day 1, 3-5 hours	45.9083 (± 44.8309)	61.7426 (± 51.2924)		

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma concentrations of metabolite AZ7550

End point title	Plasma concentrations of metabolite AZ7550[4]

End point description:

To characterise the pharmacokinetics (PK) of osimertinib metabolite AZ7550. Here arbitrary number "9999.9999" reflects that the values were non-quantifiable and not calculable.

End point type	Secondary

End point timeframe:

Blood samples collected from each participant at pre-dose, 0.5 to 2 hours, and 3 to 5 hours post-dose on Day 1 Cycle 1, and every other cycle thereafter up to and including Cycle 13 (approximately 9 months)

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analyses have been performed

End point values	Osimertinib 80 mg (Global Cohort)	Osimertinib 80 mg (China Cohort)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	279	71		
Units: Nano moles				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 1, Predose	9999.9999 (± 9999.9999)	9999.9999 (± 9999.9999)		
Cycle 1 Day 1, 0.5 - 2 hours	0.1437 (± 168.2087)	9999.9999 (± 9999.9999)		
Cycle 1 Day 1, 3 - 5 hours	1.8610 (± 147.4624)	2.1876 (± 123.6012)		
Cycle 3 Day 1, Predose	46.1286 (± 45.1082)	55.9958 (± 50.5705)		
Cycle 3 Day 1, 0.5 - 2 hours	46.0045 (± 45.9584)	55.6754 (± 53.0925)		
Cycle 3 Day 1, 3 - 5 hours	51.7182 (± 45.3240)	62.3493 (± 53.5513)		
Cycle 5 Day 1, Predose	44.4537 (± 54.9882)	53.0434 (± 52.2936)		
Cycle 5 Day 1, 0.5 - 2 hours	45.2186 (± 51.6418)	53.1901 (± 51.5506)		
Cycle 5 Day 1, 3-5 hours	51.4018 (± 51.3627)	62.5218 (± 51.0627)		
Cycle 7 Day 1, Predose	46.2912 (± 49.8713)	53.4167 (± 50.8399)		
Cycle 7 Day 1, 0.5-2 hours	46.3540 (± 49.0845)	54.3942 (± 46.1253)		
Cycle 7 Day 1,3-5 hours	52.3533 (± 47.6489)	61.9004 (± 51.6117)		

Cycle 9 Day 1, Predose	49.6058 (± 45.5050)	54.8207 (± 50.2534)		
Cycle 9 Day 1, 0.5-2 hours	49.9381 (± 46.4568)	55.2437 (± 52.5736)		
Cycle 9 Day 1, 3-5 hours	56.5354 (± 45.6736)	60.8933 (± 50.3474)		
Cycle 11 Day 1, Predose	50.9710 (± 46.8840)	56.4643 (± 51.2351)		
Cycle 11 Day 1, 0.5- 2 hours	51.9773 (± 45.3186)	57.4778 (± 47.3639)		
Cycle 11 Day 1, 3- 5 hours	57.6986 (± 48.2382)	65.3053 (± 49.6916)		
Cycle 13 Day 1, Predose	54.5238 (± 43.8481)	56.0666 (± 51.2464)		
Cycle 13 Day 1, 0.5-2 hours	54.1224 (± 43.7869)	56.8750 (± 47.4338)		
Cycle 13 Day 1, 3-5 hours	61.6053 (± 42.2947)	63.3365 (± 46.3082)		

Statistical analyses

No statistical analyses for this end point

Secondary: Subjects Reported Outcome by Cancer Therapy Satisfaction Questionnaire 16 items (CTSQ-16 Questionnaire)

End point title	Subjects Reported Outcome by Cancer Therapy Satisfaction Questionnaire 16 items (CTSQ-16 Questionnaire)

End point description:

The CTSQ-16 was a 16-item questionnaire measuring 3 domains related to subject's satisfaction with cancer therapy: Expectations of therapy, Feelings about side effects, and Satisfaction with therapy. Scores ranged from 0 to 100 for each domain, with a higher score associated with the best outcome on each domain. The results of the analyses were presented in terms of mean together with standard deviation.

End point type	Secondary

End point timeframe:

Questionnaire completed in cycle 2 and 3, prior to Week 6 scan (approximately 2 months)

End point values	Osimertinib 80 mg (Global Cohort)	SoC EGFR-TKI (Global Cohort)	Osimertinib 80 mg (China Cohort)	SoC EGFR-TKI (China Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	279	277	71	65
Units: Unit on scale				
arithmetic mean (standard deviation)				
Expectations with Therapy, Week 3	74.1 (± 22.42)	70.3 (± 21.85)	77.1 (± 20.60)	79.2 (± 18.58)
Expectations with Therapy, Week 6	76.3 (± 20.58)	74.0 (± 19.46)	82.2 (± 17.88)	82.6 (± 17.95)
Feelings about Side-Effects, Week 3	74.5 (± 17.22)	69.1 (± 20.96)	73.3 (± 19.89)	72.5 (± 17.46)
Feelings about Side-Effects, Week 6	74.6 (± 19.83)	69.9 (± 20.73)	69.0 (± 24.46)	69.7 (± 20.99)
Satisfaction with Therapy, Week 3	84.4 (± 12.88)	82.6 (± 13.60)	87.2 (± 12.14)	86.6 (± 11.07)
Satisfaction with Therapy, Week 6	84.2 (± 13.94)	84.6 (± 12.38)	87.4 (± 13.29)	87.2 (± 12.06)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life (QLQ) Questionnaires Lung Cancer 13 (QLQ-LC13)

End point title	Change from baseline in European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life (QLQ) Questionnaires Lung Cancer 13 (QLQ-LC13)

End point description:

The EORTC QLQ-LC13 was a lung-cancer-specific module comprising 13 questions to assess lung cancer symptoms (cough, haemoptysis, dyspnoea, and site-specific pain); treatment related side-effects (sore mouth, dysphagia, peripheral neuropathy, and alopecia); and pain medication. An outcome variable consisting of a score from 0 to 100 was derived for each of the symptom scales/symptom items. Higher scores on the global health status/QoL and functioning scales indicated better health status/QoL and function. Higher scores on the symptoms scales indicated greater symptom burden. The analysis was performed using a Mixed-effects model for repeated measures analysis on the change from baseline in PRO symptom score at each visit up to 9 months (281 days), including subjects, treatment, visit and treatment by visit interaction as explanatory variables, the baseline PRO score as a covariate along with the baseline PRO score by visit interaction, using an unstructured covariance structure.

End point type	Secondary

End point timeframe:

Questionnaires completed at baseline, first 9 months, and at week 1, 2, 3, 4, 5, 6, 12, 18, 24, 30 and 36

End point values	Osimertinib 80 mg (Global Cohort)	SoC EGFR-TKI (Global Cohort)	Osimertinib 80 mg (China Cohort)	SoC EGFR-TKI (China Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	279	277	71	65
Units: Unit on scale				
least squares mean (confidence interval 95%)				
Dyspnoea, First 9 months	-4.04 (-5.63 to -2.45)	-4.14 (-5.73 to -2.54)	-4.87 (-7.81 to -1.92)	-4.82 (-8.01 to -1.63)
Dyspnoea, week 1	-3.46 (-5.12 to -1.81)	-3.60 (-5.24 to -1.96)	-1.61 (-5.03 to 1.81)	0.68 (-3.03 to 4.39)
Dyspnoea, week 2	-3.94 (-5.87 to -2.00)	-3.64 (-5.57 to -1.70)	-2.27 (-6.01 to 1.48)	-5.03 (-9.08 to -0.98)
Dyspnoea, week 3	-3.99 (-5.85 to -2.12)	-3.27 (-5.14 to -1.41)	-3.09 (-6.96 to 0.77)	-5.55 (-9.69 to -1.42)
Dyspnoea, week 4	-4.81 (-6.59 to -3.02)	-4.11 (-5.88 to -2.34)	-5.35 (-8.72 to -1.99)	-5.55 (-9.20 to -1.89)
Dyspnoea, week 5	-3.51 (-5.53 to -1.50)	-5.19 (-7.22 to -3.17)	-5.72 (-10.06 to -1.39)	-5.76 (-10.32 to -1.20)
Dyspnoea, week 6	-4.51 (-6.47 to -2.56)	-4.45 (-6.42 to -2.48)	-4.83 (-8.53 to -1.12)	-6.37 (-10.40 to -2.33)
Dyspnoea, week 12	-3.83 (-5.99 to -1.68)	-5.75 (-7.96 to -3.54)	-5.38 (-9.41 to -1.35)	-6.67 (-11.04 to -2.30)

Dyspnoea, week 18	-4.97 (-7.18 to -2.76)	-5.21 (-7.46 to -2.95)	-7.67 (-11.54 to -3.79)	-7.48 (-11.66 to -3.30)
Dyspnoea, week 24	-4.65 (-7.06 to -2.25)	-4.56 (-7.02 to -2.09)	-7.59 (-11.84 to -3.34)	-5.67 (-10.27 to -1.08)
Dyspnoea, week 30	-3.89 (-6.34 to -1.45)	-3.68 (-6.22 to -1.15)	-5.81 (-10.59 to -1.02)	-3.46 (-8.58 to 1.65)
Dyspnoea, week 36	-2.88 (-5.52 to -0.24)	-2.04 (-4.83 to 0.75)	-4.21 (-8.91 to 0.48)	-2.18 (-7.28 to 2.93)
Cough, First 9 months	-10.97 (-12.77 to -9.17)	-11.65 (-13.47 to -9.84)	-13.75 (-17.17 to -10.33)	-8.49 (-12.19 to -4.79)
Cough, week 1	-6.90 (-9.30 to -4.51)	-4.83 (-7.20 to -2.46)	-4.60 (-9.00 to -0.20)	-3.69 (-8.46 to 1.07)
Cough, week 2	-9.04 (-11.58 to -6.49)	-9.52 (-12.05 to -6.98)	-12.26 (-17.15 to -7.37)	-3.73 (-9.01 to 1.54)
Cough, week 3	-9.78 (-12.37 to -7.20)	-10.24 (-12.82 to -7.65)	-11.95 (-16.66 to -7.24)	-5.56 (-10.57 to -0.54)
Cough, week 4	-11.25 (-13.87 to -8.63)	-13.36 (-15.96 to -10.76)	-12.78 (-17.80 to -7.77)	-10.32 (-15.75 to -4.90)
Cough, week 5	-12.98 (-15.64 to -10.31)	-13.55 (-16.21 to -10.88)	-17.74 (-23.11 to -12.38)	-9.20 (-14.84 to -3.55)
Cough, week 6	-11.88 (-14.56 to -9.19)	-11.92 (-14.63 to -9.21)	-16.92 (-22.36 to -11.48)	-10.58 (-16.52 to -4.64)
Cough, week 12	-13.36 (-15.95 to -10.78)	-13.57 (-16.24 to -10.90)	-15.51 (-21.39 to -9.64)	-8.04 (-14.41 to -1.67)
Cough, week 18	-12.31 (-15.25 to -9.37)	-11.00 (-14.03 to -7.98)	-11.79 (-17.19 to -6.40)	-9.44 (-15.23 to -3.65)
Cough, week 24	-11.34 (-14.24 to -8.43)	-13.16 (-16.17 to -10.14)	-17.61 (-22.84 to -12.39)	-14.92 (-20.56 to -9.29)
Cough, week 30	-10.34 (-13.21 to -7.46)	-12.43 (-15.44 to -9.41)	-15.45 (-21.46 to -9.45)	-9.35 (-15.75 to -2.94)
Cough, week 36	-11.49 (-14.48 to -8.49)	-14.62 (-17.85 to -11.39)	-14.62 (-20.65 to -8.58)	-8.55 (-15.14 to -1.96)
Pain in Chest, First 9 months	-6.62 (-8.24 to -5.01)	-6.41 (-8.04 to -4.78)	-2.79 (-5.84 to 0.26)	-4.74 (-8.05 to -1.44)
Pain in Chest, week 1	-1.93 (-4.19 to 0.32)	-4.26 (-6.50 to -2.03)	-1.79 (-5.98 to 2.40)	-4.16 (-8.71 to 0.38)
Pain in Chest, week 2	-5.94 (-8.13 to -3.74)	-6.32 (-8.51 to -4.13)	-4.76 (-8.63 to -0.89)	-3.00 (-7.18 to 1.17)
Pain in Chest, week 3	-7.17 (-9.31 to -5.04)	-5.36 (-7.49 to -3.23)	-0.76 (-4.90 to 3.39)	-4.77 (-9.18 to -0.36)
Pain in Chest, week 4	-7.45 (-9.60 to -5.29)	-6.40 (-8.54 to -4.26)	-2.13 (-6.32 to 2.07)	-4.22 (-8.78 to 0.34)
Pain in Chest, week 5	-7.33 (-9.54 to -5.11)	-6.98 (-9.20 to -4.76)	-0.62 (-4.67 to 3.42)	-6.82 (-11.05 to -2.60)
Pain in Chest, week 6	-4.99 (-7.30 to -2.68)	-7.08 (-9.41 to -4.75)	0.94 (-3.40 to 5.29)	-6.26 (-11.00 to -1.52)
Pain in Chest, week 12	-7.28 (-9.56 to -5.01)	-6.70 (-9.05 to -4.35)	-3.71 (-8.77 to 1.35)	-5.13 (-10.62 to 0.36)
Pain in Chest, week 18	-6.79 (-9.22 to -4.36)	-7.90 (-10.40 to -5.41)	-4.40 (-9.05 to 0.26)	-7.24 (-12.23 to -2.25)
Pain in Chest, week 24	-7.72 (-10.26 to -5.18)	-7.34 (-9.95 to -4.72)	-5.66 (-10.48 to -0.84)	-3.15 (-8.36 to 2.07)
Pain in Chest, week 30	-8.33 (-10.80 to -5.87)	-6.60 (-9.18 to -4.02)	-4.25 (-9.62 to 1.12)	-4.02 (-9.76 to 1.72)
Pain in Chest, week 36	-7.94 (-10.59 to -5.30)	-5.58 (-8.43 to -2.73)	-3.56 (-9.42 to 2.30)	-3.40 (-9.80 to 3.00)

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline in European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items (EORTC QLQ-C30)

End point title	Change from baseline in European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items (EORTC QLQ-C30)

End point description:

The EORTC QLQ-C30 cancer-specific questionnaire consisted of 30 questions, combined to produce 5 functional scales, 3 symptom scales, 6 individual items, and a global measure of health status/QoL. An outcome variable consisting of a score from 0 to 100 was derived for each of the symptom scales/symptom items, the functional scales, and the global health status/QoL scale in the EORTC QLQ-C30. Higher scores on the global health status and functioning scales indicated better health status/function. Higher scores on the symptoms scales indicated greater symptom burden. The analysis was performed using a Mixed-effects model for repeated measures analysis on the change from baseline in PRO symptom score at each visit up to 9 months (281 days), including subjects, treatment, visit and treatment by visit interaction as explanatory variables, the baseline PRO score as a covariate along with the baseline PRO score by visit interaction, using an unstructured covariance structure.

End point type	Secondary

End point timeframe:

Questionnaires completed at baseline, first 9 months, and at week 6, 12, 18, 24, 30, and 36.

End point values	Osimertinib 80 mg (Global Cohort)	SoC EGFR-TKI (Global Cohort)	Osimertinib 80 mg (China Cohort)	SoC EGFR-TKI (China Cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	279	277	71	65
Units: Unit on scale				
least squares mean (confidence interval 95%)				
Fatigue, First 9 months	-5.48 (-7.45 to -3.52)	-4.72 (-6.74 to -2.69)	-5.65 (-9.33 to -1.98)	-5.79 (-9.58 to -2.00)
Fatigue, week 6	-4.13 (-6.35 to -1.91)	-5.78 (-8.02 to -3.54)	-1.73 (-6.05 to 2.58)	-6.81 (-11.30 to -2.33)
Fatigue, week 12	-5.11 (-7.31 to -2.91)	-6.52 (-8.81 to -4.23)	-5.40 (-9.51 to -1.29)	-6.36 (-10.61 to -2.12)
Fatigue, week 18	-6.83 (-9.21 to -4.44)	-5.77 (-8.23 to -3.31)	-6.64 (-11.26 to -2.03)	-7.90 (-12.61 to -3.19)
Fatigue, week 24	-6.18 (-8.75 to -3.61)	-4.96 (-7.63 to -2.28)	-8.92 (-13.30 to -4.54)	-3.87 (-8.32 to 0.58)
Fatigue, week 30	-5.19 (-7.94 to -2.43)	-3.26 (-6.16 to -0.35)	-4.43 (-9.53 to 0.68)	-6.31 (-11.53 to -1.10)
Fatigue, week 36	-5.47 (-8.31 to -2.63)	-2.00 (-2.00 to 1.04)	-6.78 (-12.38 to -1.19)	-3.46 (-9.28 to 2.36)
Appetite Loss, First 9 months	-6.15 (-8.39 to -3.90)	-5.64 (-7.96 to -3.32)	1.18 (-2.78 to 5.14)	-1.73 (-5.80 to 2.34)
Appetite Loss, week 6	-4.54 (-7.36 to -1.72)	-5.67 (-8.52 to -2.83)	3.20 (-1.60 to 8.01)	-6.27 (-11.26 to -1.27)
Appetite Loss, week 12	-6.52 (-9.43 to -3.62)	-6.95 (-9.98 to -3.91)	1.58 (-3.23 to 6.39)	-1.44 (-6.41 to 3.53)
Appetite Loss, week 18	-7.27 (-10.09 to -4.45)	-6.84 (-9.75 to -3.92)	1.42 (-4.38 to 7.22)	-4.43 (-10.35 to 1.48)
Appetite Loss, week 24	-7.14 (-10.27 to -4.01)	-5.08 (-8.35 to -1.81)	-2.26 (-7.74 to 3.22)	0.24 (-5.29 to 5.78)
Appetite Loss, week 30	-4.50 (-7.74 to -1.26)	-4.17 (-7.60 to -0.74)	2.19 (-3.28 to 7.65)	-1.83 (-7.36 to 3.70)

Appetite Loss, week 36	-6.90 (-10.00 to -3.81)	-5.15 (-8.49 to -1.81)	0.98 (-5.28 to 7.24)	3.36 (-3.15 to 9.86)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All adverse events (AEs) were collected from the time of signature of informed consent throughout the Treatment Period and including the safety follow-up period.The safety follow-up period was defined as 28 days after study drug was discontinued.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups

Reporting group title	Osimertinib 80 mg (Global Cohort)

Reporting group description:

Randomized participants received Osimertinib 80 mg orally once daily (QD)

Reporting group title	SoC EGFR-TKI (China Cohort)

Reporting group description:

Randomized participant received Standard of care (SoC) Epidermal growth factor receptor-tyrosine kinase inhibitor (EGFRTKI). Participants received gefitinib 250 mg orally QD or erlotinib 150 mg orally QD.

Reporting group title	SoC EGFR-TKI (Global Cohort)

Reporting group description:

Randomized participant received Standard of care (SoC) Epidermal growth factor receptor-tyrosine kinase inhibitor (EGFR-TKI). Participants received gefitinib 250 mg orally QD or erlotinib 150 mg orally QD.

Reporting group title	Osimertinib 80 mg (China Cohort)

Reporting group description:

Randomized participants received Osimertinib 80 mg orally once daily (QD)

Serious adverse events	Osimertinib 80 mg (Global Cohort)	SoC EGFR-TKI (China Cohort)	SoC EGFR-TKI (Global Cohort)
Total subjects affected by serious adverse events			
subjects affected / exposed	74 / 279 (26.52%)	12 / 65 (18.46%)	76 / 277 (27.44%)
number of deaths (all causes)	155	44	166
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Endometrial adenocarcinoma			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Histiocytic necrotising lymphadenitis			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Invasive ductal breast carcinoma			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian fibroma			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine leiomyoma			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Desmoid tumour			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder cancer			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Circulatory collapse			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Aortic dissection			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolism			

subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep vein thrombosis			
subjects affected / exposed	2 / 279 (0.72%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombophlebitis			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral artery occlusion			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orthostatic hypotension			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Venous thrombosis limb			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Venous thrombosis			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Condition aggravated			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			

subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthenia			
subjects affected / exposed	2 / 279 (0.72%)	0 / 65 (0.00%)	2 / 277 (0.72%)
occurrences causally related to treatment / all	1 / 2	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug withdrawal syndrome			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
General physical health deterioration			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	3 / 279 (1.08%)	0 / 65 (0.00%)	2 / 277 (0.72%)
occurrences causally related to treatment / all	3 / 3	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Uterine polyp			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Benign prostatic hyperplasia			

subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	2 / 279 (0.72%)	0 / 65 (0.00%)	2 / 277 (0.72%)
occurrences causally related to treatment / all	0 / 2	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			
subjects affected / exposed	0 / 279 (0.00%)	1 / 65 (1.54%)	4 / 277 (1.44%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Hypoxia			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Interstitial lung disease			
subjects affected / exposed	4 / 279 (1.43%)	1 / 65 (1.54%)	3 / 277 (1.08%)
occurrences causally related to treatment / all	4 / 4	1 / 1	3 / 3
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Pleural effusion			
subjects affected / exposed	4 / 279 (1.43%)	1 / 65 (1.54%)	3 / 277 (1.08%)
occurrences causally related to treatment / all	0 / 4	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	2 / 279 (0.72%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	2 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			

subjects affected / exposed	2 / 279 (0.72%)	0 / 65 (0.00%)	2 / 277 (0.72%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	4 / 279 (1.43%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pulmonary haemorrhage			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	2 / 277 (0.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Tonsillolith			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchiectasis			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Acute psychosis			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Confusional state			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			

subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alanine aminotransferase increased			
subjects affected / exposed	1 / 279 (0.36%)	1 / 65 (1.54%)	2 / 277 (0.72%)
occurrences causally related to treatment / all	1 / 1	1 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Platelet count decreased			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transaminases increased			
subjects affected / exposed	1 / 279 (0.36%)	1 / 65 (1.54%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood bilirubin increased			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
White blood cell count decreased			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			

Fall			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	2 / 277 (0.72%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral neck fracture			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Procedural pneumothorax			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head injury			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound complication			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wrist fracture			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Poisoning			

subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bundle branch block left			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac tamponade			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			

subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Tachyarrhythmia			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure chronic			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericarditis			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Nervous system disorders			
Brain oedema			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral infarction			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cognitive disorder			

subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Depressed level of consciousness			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhagic stroke			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Migraine			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral motor neuropathy			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal cord compression			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			

subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	0 / 279 (0.00%)	1 / 65 (1.54%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral ventricle dilatation			
subjects affected / exposed	0 / 279 (0.00%)	1 / 65 (1.54%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral ischaemia			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood disorder			

subjects affected / exposed	0 / 279 (0.00%)	1 / 65 (1.54%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Neutropenia			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 279 (0.72%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic gastritis			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	3 / 279 (1.08%)	0 / 65 (0.00%)	4 / 277 (1.44%)
occurrences causally related to treatment / all	3 / 4	0 / 0	2 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Enterocolitis			
subjects affected / exposed	2 / 279 (0.72%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis erosive			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			

subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Haemorrhoidal haemorrhage			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal ischaemia			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Melaena			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mouth ulceration			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	2 / 277 (0.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	5 / 277 (1.81%)
occurrences causally related to treatment / all	1 / 1	0 / 0	4 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper gastrointestinal haemorrhage			

subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer			
subjects affected / exposed	0 / 279 (0.00%)	1 / 65 (1.54%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower gastrointestinal haemorrhage			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophagitis			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Drug-induced liver injury			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	3 / 277 (1.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			
subjects affected / exposed	0 / 279 (0.00%)	1 / 65 (1.54%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic function abnormal			

subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Dermatitis acneiform			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	2 / 277 (0.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxic epidermal necrolysis			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erythema nodosum			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	2 / 279 (0.72%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Ureterolithiasis			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Inappropriate antidiuretic hormone secretion			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Hypothyroidism			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Flank pain			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pathological fracture			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rotator cuff syndrome			
subjects affected / exposed	1 / 279 (0.36%)	1 / 65 (1.54%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone pain			
subjects affected / exposed	0 / 279 (0.00%)	1 / 65 (1.54%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neck pain			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Infections and infestations			
Anal abscess			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridial infection			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacteraemia			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile infection			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	2 / 277 (0.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea infectious			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Empyema			

subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocarditis			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Enteritis infectious			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia urinary tract infection			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile infection			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	2 / 279 (0.72%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection viral			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Perineal abscess			

subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngotonsillitis			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural infection			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	9 / 279 (3.23%)	1 / 65 (1.54%)	7 / 277 (2.53%)
occurrences causally related to treatment / all	0 / 9	0 / 1	1 / 7
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 2
Pneumonia mycoplasmal			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal abscess			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Salmonella bacteraemia			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			

subjects affected / exposed	3 / 279 (1.08%)	0 / 65 (0.00%)	3 / 277 (1.08%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 2
Sinusitis			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tracheobronchitis			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adenoviral upper respiratory infection			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 279 (0.00%)	1 / 65 (1.54%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung infection			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis C			

subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia pseudomonal			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia viral			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural infection			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus bronchitis			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 279 (0.72%)	0 / 65 (0.00%)	2 / 277 (0.72%)
occurrences causally related to treatment / all	0 / 2	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic ketoacidosis			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			

subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	4 / 279 (1.43%)	0 / 65 (0.00%)	1 / 277 (0.36%)
occurrences causally related to treatment / all	1 / 4	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperuricaemia			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour lysis syndrome			
subjects affected / exposed	0 / 279 (0.00%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	1 / 279 (0.36%)	0 / 65 (0.00%)	0 / 277 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Osimertinib 80 mg (China Cohort)		
Total subjects affected by serious adverse events			
subjects affected / exposed	25 / 71 (35.21%)		
number of deaths (all causes)	45		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Endometrial adenocarcinoma			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Histiocytic necrotising lymphadenitis			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Invasive ductal breast carcinoma				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ovarian fibroma				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Prostate cancer				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Uterine leiomyoma				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Desmoid tumour				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bladder cancer				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Circulatory collapse				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Aortic dissection				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Embolism				

subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Deep vein thrombosis				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Thrombophlebitis				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peripheral artery occlusion				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Orthostatic hypotension				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Venous thrombosis limb				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Venous thrombosis				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Condition aggravated				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chest pain				

subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Asthenia				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Drug withdrawal syndrome				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Fatigue				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Death				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			
General physical health deterioration				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast disorders				
Uterine polyp				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Benign prostatic hyperplasia				

subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Asthma			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haemoptysis			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypoxia			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Interstitial lung disease			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pleural effusion			
subjects affected / exposed	3 / 71 (4.23%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Pneumonitis			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumothorax			

subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary haemorrhage				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory failure				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Tonsillolith				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchiectasis				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Acute psychosis				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Confusional state				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Depression				

subjects affected / exposed	1 / 71 (1.41%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Investigations				
Electrocardiogram QT prolonged				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Aspartate aminotransferase increased				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Alanine aminotransferase increased				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Platelet count decreased				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Transaminases increased				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood bilirubin increased				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
White blood cell count decreased				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				

Fall				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Femoral neck fracture				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Femur fracture				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Procedural pneumothorax				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Head injury				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Subdural haematoma				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Wound complication				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Wrist fracture				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Poisoning				

subjects affected / exposed	1 / 71 (1.41%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Cardiac disorders				
Acute myocardial infarction				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Angina pectoris				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atrial fibrillation				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Bundle branch block left				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac arrest				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Cardiac failure				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac tamponade				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			
Myocardial infarction				

subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tachyarrhythmia				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pericardial effusion				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac failure chronic				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pericarditis				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Brain oedema				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebral infarction				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cerebrovascular accident				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cognitive disorder				

subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Depressed level of consciousness				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dizziness				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemorrhagic stroke				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ischaemic stroke				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Migraine				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peripheral motor neuropathy				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Spinal cord compression				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Seizure				

subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Transient ischaemic attack				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Subarachnoid haemorrhage				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Epilepsy				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebral ventricle dilatation				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebral ischaemia				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Anaemia				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancytopenia				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood disorder				

subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neutropenia				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Ear and labyrinth disorders				
Vertigo				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Abdominal pain				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chronic gastritis				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Enterocolitis				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastritis erosive				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal haemorrhage				

subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemorrhoidal haemorrhage				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Inguinal hernia				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intestinal ischaemia				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Melaena				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Mouth ulceration				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Stomatitis				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Upper gastrointestinal haemorrhage				

subjects affected / exposed	1 / 71 (1.41%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			
Duodenal ulcer				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Abdominal pain upper				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lower gastrointestinal haemorrhage				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oesophagitis				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancreatitis				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Drug-induced liver injury				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholecystitis				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatic function abnormal				

subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Dermatitis acneiform			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Toxic epidermal necrolysis			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Erythema nodosum			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal failure			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ureterolithiasis			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Inappropriate antidiuretic hormone secretion			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Hypothyroidism				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Back pain				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Flank pain				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal chest pain				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pathological fracture				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rotator cuff syndrome				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bone pain				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Neck pain				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Infections and infestations			
Anal abscess			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Clostridial infection			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bacteraemia			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Clostridium difficile infection			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cystitis			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Device related infection			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diarrhoea infectious			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diverticulitis			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Empyema			

subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Endocarditis				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Enteritis infectious				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Escherichia urinary tract infection				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Febrile infection				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lower respiratory tract infection				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lower respiratory tract infection viral				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Perineal abscess				

subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pharyngotonsillitis				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pleural infection				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	3 / 71 (4.23%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Pneumonia mycoplasmal				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rectal abscess				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory tract infection				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Salmonella bacteraemia				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sepsis				

subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sinusitis				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tracheobronchitis				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchitis				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Adenoviral upper respiratory infection				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Upper respiratory tract infection				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lung infection				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatitis C				

subjects affected / exposed	1 / 71 (1.41%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia pseudomonal				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia viral				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Post procedural infection				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory syncytial virus bronchitis				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Decreased appetite				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diabetic ketoacidosis				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hyperglycaemia				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypoglycaemia				

subjects affected / exposed	1 / 71 (1.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyperuricaemia			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tumour lysis syndrome			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Dehydration			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Osimertinib 80 mg (Global Cohort)	SoC EGFR-TKI (China Cohort)	SoC EGFR-TKI (Global Cohort)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	273 / 279 (97.85%)	64 / 65 (98.46%)	269 / 277 (97.11%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
subjects affected / exposed	14 / 279 (5.02%)	0 / 65 (0.00%)	7 / 277 (2.53%)
occurrences (all)	18	0	7
Vascular disorders			
Hypertension			
subjects affected / exposed	15 / 279 (5.38%)	5 / 65 (7.69%)	10 / 277 (3.61%)
occurrences (all)	18	5	12
General disorders and administration			

site conditions			
Fatigue			
subjects affected / exposed	45 / 279 (16.13%)	6 / 65 (9.23%)	34 / 277 (12.27%)
occurrences (all)	53	8	41
Pyrexia			
subjects affected / exposed	29 / 279 (10.39%)	3 / 65 (4.62%)	10 / 277 (3.61%)
occurrences (all)	37	4	12
Oedema peripheral			
subjects affected / exposed	16 / 279 (5.73%)	0 / 65 (0.00%)	24 / 277 (8.66%)
occurrences (all)	19	0	27
Asthenia			
subjects affected / exposed	25 / 279 (8.96%)	3 / 65 (4.62%)	9 / 277 (3.25%)
occurrences (all)	34	3	9
Chest discomfort			
subjects affected / exposed	5 / 279 (1.79%)	8 / 65 (12.31%)	2 / 277 (0.72%)
occurrences (all)	5	10	2
Non-cardiac chest pain			
subjects affected / exposed	18 / 279 (6.45%)	5 / 65 (7.69%)	17 / 277 (6.14%)
occurrences (all)	18	5	17
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	60 / 279 (21.51%)	11 / 65 (16.92%)	50 / 277 (18.05%)
occurrences (all)	77	14	60
Dyspnoea			
subjects affected / exposed	40 / 279 (14.34%)	5 / 65 (7.69%)	21 / 277 (7.58%)
occurrences (all)	47	5	21
Epistaxis			
subjects affected / exposed	21 / 279 (7.53%)	0 / 65 (0.00%)	14 / 277 (5.05%)
occurrences (all)	54	0	28
Haemoptysis			
subjects affected / exposed	7 / 279 (2.51%)	3 / 65 (4.62%)	16 / 277 (5.78%)
occurrences (all)	7	3	16
Pleural effusion			
subjects affected / exposed	0 / 279 (0.00%)	2 / 65 (3.08%)	0 / 277 (0.00%)
occurrences (all)	0	2	0
Productive cough			

subjects affected / exposed	13 / 279 (4.66%)	2 / 65 (3.08%)	6 / 277 (2.17%)
occurrences (all)	19	2	6
Oropharyngeal pain			
subjects affected / exposed	14 / 279 (5.02%)	1 / 65 (1.54%)	12 / 277 (4.33%)
occurrences (all)	19	1	15
Psychiatric disorders			
Insomnia			
subjects affected / exposed	31 / 279 (11.11%)	5 / 65 (7.69%)	21 / 277 (7.58%)
occurrences (all)	31	5	24
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	27 / 279 (9.68%)	28 / 65 (43.08%)	68 / 277 (24.55%)
occurrences (all)	32	38	82
Alanine aminotransferase increased			
subjects affected / exposed	18 / 279 (6.45%)	29 / 65 (44.62%)	72 / 277 (25.99%)
occurrences (all)	18	39	85
Electrocardiogram QT prolonged			
subjects affected / exposed	27 / 279 (9.68%)	3 / 65 (4.62%)	12 / 277 (4.33%)
occurrences (all)	46	4	15
Weight decreased			
subjects affected / exposed	20 / 279 (7.17%)	8 / 65 (12.31%)	20 / 277 (7.22%)
occurrences (all)	24	9	24
White blood cell count decreased			
subjects affected / exposed	27 / 279 (9.68%)	6 / 65 (9.23%)	5 / 277 (1.81%)
occurrences (all)	51	10	6
Blood alkaline phosphatase increased			
subjects affected / exposed	7 / 279 (2.51%)	4 / 65 (6.15%)	15 / 277 (5.42%)
occurrences (all)	7	6	19
Platelet count decreased			
subjects affected / exposed	14 / 279 (5.02%)	1 / 65 (1.54%)	3 / 277 (1.08%)
occurrences (all)	18	2	4
Neutrophil count decreased			
subjects affected / exposed	12 / 279 (4.30%)	3 / 65 (4.62%)	2 / 277 (0.72%)
occurrences (all)	29	4	2
Lymphocyte count decreased			

subjects affected / exposed	9 / 279 (3.23%)	3 / 65 (4.62%)	1 / 277 (0.36%)
occurrences (all)	9	4	1
Gamma-glutamyltransferase increased			
subjects affected / exposed	10 / 279 (3.58%)	7 / 65 (10.77%)	2 / 277 (0.72%)
occurrences (all)	11	10	2
Blood bilirubin increased			
subjects affected / exposed	7 / 279 (2.51%)	6 / 65 (9.23%)	13 / 277 (4.69%)
occurrences (all)	13	9	18
Blood albumin decreased			
subjects affected / exposed	1 / 279 (0.36%)	3 / 65 (4.62%)	2 / 277 (0.72%)
occurrences (all)	2	4	3
Blood creatinine increased			
subjects affected / exposed	11 / 279 (3.94%)	2 / 65 (3.08%)	4 / 277 (1.44%)
occurrences (all)	14	2	5
Blood lactate dehydrogenase increased			
subjects affected / exposed	3 / 279 (1.08%)	2 / 65 (3.08%)	3 / 277 (1.08%)
occurrences (all)	3	3	4
Haemoglobin decreased			
subjects affected / exposed	4 / 279 (1.43%)	4 / 65 (6.15%)	2 / 277 (0.72%)
occurrences (all)	4	4	2
Blood uric acid increased			
subjects affected / exposed	0 / 279 (0.00%)	1 / 65 (1.54%)	0 / 277 (0.00%)
occurrences (all)	0	3	0
Injury, poisoning and procedural complications			
Injury, poisoning and procedural complications			
subjects affected / exposed	33 / 279 (11.83%)	1 / 65 (1.54%)	29 / 277 (10.47%)
occurrences (all)	43	1	33
Cardiac disorders			
Left ventricular dysfunction			
subjects affected / exposed	0 / 279 (0.00%)	5 / 65 (7.69%)	2 / 277 (0.72%)
occurrences (all)	0	5	2
Nervous system disorders			
Headache			

subjects affected / exposed	39 / 279 (13.98%)	4 / 65 (6.15%)	25 / 277 (9.03%)
occurrences (all)	53	6	29
Dysgeusia			
subjects affected / exposed	18 / 279 (6.45%)	0 / 65 (0.00%)	9 / 277 (3.25%)
occurrences (all)	19	0	9
Dizziness			
subjects affected / exposed	22 / 279 (7.89%)	4 / 65 (6.15%)	12 / 277 (4.33%)
occurrences (all)	25	5	13
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	44 / 279 (15.77%)	11 / 65 (16.92%)	26 / 277 (9.39%)
occurrences (all)	53	12	32
Thrombocytopenia			
subjects affected / exposed	26 / 279 (9.32%)	1 / 65 (1.54%)	0 / 277 (0.00%)
occurrences (all)	37	1	0
Leukopenia			
subjects affected / exposed	21 / 279 (7.53%)	2 / 65 (3.08%)	3 / 277 (1.08%)
occurrences (all)	34	3	3
Neutropenia			
subjects affected / exposed	21 / 279 (7.53%)	2 / 65 (3.08%)	1 / 277 (0.36%)
occurrences (all)	35	2	1
Bone marrow failure			
subjects affected / exposed	1 / 279 (0.36%)	4 / 65 (6.15%)	1 / 277 (0.36%)
occurrences (all)	3	7	2
Ear and labyrinth disorders			
Ear and labyrinth disorders			
subjects affected / exposed	17 / 279 (6.09%)	1 / 65 (1.54%)	14 / 277 (5.05%)
occurrences (all)	22	1	16
Eye disorders			
Dry eye			
subjects affected / exposed	21 / 279 (7.53%)	1 / 65 (1.54%)	21 / 277 (7.58%)
occurrences (all)	50	2	42
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	167 / 279 (59.86%)	19 / 65 (29.23%)	159 / 277 (57.40%)
occurrences (all)	262	31	246
Stomatitis			

subjects affected / exposed	82 / 279 (29.39%)	1 / 65 (1.54%)	60 / 277 (21.66%)
occurrences (all)	118	1	73
Nausea			
subjects affected / exposed	55 / 279 (19.71%)	7 / 65 (10.77%)	55 / 277 (19.86%)
occurrences (all)	66	7	81
Constipation			
subjects affected / exposed	51 / 279 (18.28%)	3 / 65 (4.62%)	39 / 277 (14.08%)
occurrences (all)	64	5	44
Vomiting			
subjects affected / exposed	40 / 279 (14.34%)	5 / 65 (7.69%)	28 / 277 (10.11%)
occurrences (all)	50	7	36
Dry mouth			
subjects affected / exposed	12 / 279 (4.30%)	3 / 65 (4.62%)	15 / 277 (5.42%)
occurrences (all)	12	3	15
Abdominal pain			
subjects affected / exposed	12 / 279 (4.30%)	3 / 65 (4.62%)	17 / 277 (6.14%)
occurrences (all)	13	3	18
Mouth ulceration			
subjects affected / exposed	12 / 279 (4.30%)	7 / 65 (10.77%)	4 / 277 (1.44%)
occurrences (all)	20	11	4
Toothache			
subjects affected / exposed	3 / 279 (1.08%)	4 / 65 (6.15%)	1 / 277 (0.36%)
occurrences (all)	3	4	1
Abdominal pain upper			
subjects affected / exposed	16 / 279 (5.73%)	2 / 65 (3.08%)	13 / 277 (4.69%)
occurrences (all)	19	2	15
Dyspepsia			
subjects affected / exposed	8 / 279 (2.87%)	1 / 65 (1.54%)	14 / 277 (5.05%)
occurrences (all)	12	1	17
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	2 / 279 (0.72%)	5 / 65 (7.69%)	7 / 277 (2.53%)
occurrences (all)	2	6	8
Drug-induced liver injury			
subjects affected / exposed	0 / 279 (0.00%)	6 / 65 (9.23%)	2 / 277 (0.72%)
occurrences (all)	0	7	2

Skin and subcutaneous tissue disorders			
Dermatitis acneiform			
subjects affected / exposed	73 / 279 (26.16%)	9 / 65 (13.85%)	135 / 277 (48.74%)
occurrences (all)	97	11	177
Dry skin			
subjects affected / exposed	92 / 279 (32.97%)	8 / 65 (12.31%)	92 / 277 (33.21%)
occurrences (all)	104	8	100
Pruritus			
subjects affected / exposed	50 / 279 (17.92%)	4 / 65 (6.15%)	44 / 277 (15.88%)
occurrences (all)	74	7	61
Alopecia			
subjects affected / exposed	22 / 279 (7.89%)	5 / 65 (7.69%)	35 / 277 (12.64%)
occurrences (all)	22	6	35
Skin fissures			
subjects affected / exposed	18 / 279 (6.45%)	0 / 65 (0.00%)	16 / 277 (5.78%)
occurrences (all)	21	0	18
Rash			
subjects affected / exposed	17 / 279 (6.09%)	1 / 65 (1.54%)	14 / 277 (5.05%)
occurrences (all)	19	1	20
Rash macular			
subjects affected / exposed	15 / 279 (5.38%)	0 / 65 (0.00%)	12 / 277 (4.33%)
occurrences (all)	16	0	22
Rash papular			
subjects affected / exposed	18 / 279 (6.45%)	3 / 65 (4.62%)	10 / 277 (3.61%)
occurrences (all)	30	6	11
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	4 / 279 (1.43%)	3 / 65 (4.62%)	7 / 277 (2.53%)
occurrences (all)	5	3	7
Rash maculo-papular			
subjects affected / exposed	38 / 279 (13.62%)	12 / 65 (18.46%)	46 / 277 (16.61%)
occurrences (all)	52	14	63
Erythema			
subjects affected / exposed	14 / 279 (5.02%)	0 / 65 (0.00%)	11 / 277 (3.97%)
occurrences (all)	16	0	14
Onychoclasis			

subjects affected / exposed	15 / 279 (5.38%)	0 / 65 (0.00%)	5 / 277 (1.81%)
occurrences (all)	16	0	5
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	5 / 279 (1.79%)	7 / 65 (10.77%)	1 / 277 (0.36%)
occurrences (all)	5	11	1
Haematuria			
subjects affected / exposed	5 / 279 (1.79%)	5 / 65 (7.69%)	8 / 277 (2.89%)
occurrences (all)	12	10	18
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	35 / 279 (12.54%)	6 / 65 (9.23%)	29 / 277 (10.47%)
occurrences (all)	41	10	35
Arthralgia			
subjects affected / exposed	23 / 279 (8.24%)	3 / 65 (4.62%)	21 / 277 (7.58%)
occurrences (all)	25	5	27
Musculoskeletal pain			
subjects affected / exposed	28 / 279 (10.04%)	3 / 65 (4.62%)	14 / 277 (5.05%)
occurrences (all)	32	3	16
Myalgia			
subjects affected / exposed	19 / 279 (6.81%)	0 / 65 (0.00%)	14 / 277 (5.05%)
occurrences (all)	23	0	15
Muscle spasms			
subjects affected / exposed	24 / 279 (8.60%)	0 / 65 (0.00%)	13 / 277 (4.69%)
occurrences (all)	27	0	18
Pain in extremity			
subjects affected / exposed	19 / 279 (6.81%)	3 / 65 (4.62%)	6 / 277 (2.17%)
occurrences (all)	24	4	6
Musculoskeletal chest pain			
subjects affected / exposed	19 / 279 (6.81%)	1 / 65 (1.54%)	7 / 277 (2.53%)
occurrences (all)	20	1	7
Infections and infestations			
Paronychia			
subjects affected / exposed	89 / 279 (31.90%)	2 / 65 (3.08%)	84 / 277 (30.32%)
occurrences (all)	228	6	230
Upper respiratory tract infection			

subjects affected / exposed	36 / 279 (12.90%)	2 / 65 (3.08%)	23 / 277 (8.30%)
occurrences (all)	54	2	26
Conjunctivitis			
subjects affected / exposed	18 / 279 (6.45%)	4 / 65 (6.15%)	21 / 277 (7.58%)
occurrences (all)	44	8	48
Pneumonia			
subjects affected / exposed	18 / 279 (6.45%)	2 / 65 (3.08%)	4 / 277 (1.44%)
occurrences (all)	25	2	5
Urinary tract infection			
subjects affected / exposed	16 / 279 (5.73%)	8 / 65 (12.31%)	12 / 277 (4.33%)
occurrences (all)	28	12	12
Urinary tract infection bacterial			
subjects affected / exposed	12 / 279 (4.30%)	4 / 65 (6.15%)	9 / 277 (3.25%)
occurrences (all)	15	4	9
Influenza			
subjects affected / exposed	14 / 279 (5.02%)	0 / 65 (0.00%)	5 / 277 (1.81%)
occurrences (all)	14	0	7
Lung infection			
subjects affected / exposed	11 / 279 (3.94%)	4 / 65 (6.15%)	2 / 277 (0.72%)
occurrences (all)	11	5	2
Nasopharyngitis			
subjects affected / exposed	31 / 279 (11.11%)	1 / 65 (1.54%)	16 / 277 (5.78%)
occurrences (all)	64	1	23
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	64 / 279 (22.94%)	8 / 65 (12.31%)	56 / 277 (20.22%)
occurrences (all)	78	8	64
Hypokalaemia			
subjects affected / exposed	13 / 279 (4.66%)	8 / 65 (12.31%)	19 / 277 (6.86%)
occurrences (all)	18	8	22
Hypoalbuminaemia			
subjects affected / exposed	9 / 279 (3.23%)	6 / 65 (9.23%)	8 / 277 (2.89%)
occurrences (all)	13	6	12
Hypocalcaemia			
subjects affected / exposed	7 / 279 (2.51%)	7 / 65 (10.77%)	7 / 277 (2.53%)
occurrences (all)	8	9	9

Hyponatraemia			
subjects affected / exposed	15 / 279 (5.38%)	0 / 65 (0.00%)	9 / 277 (3.25%)
occurrences (all)	19	0	16
Hypoproteinaemia			
subjects affected / exposed	0 / 279 (0.00%)	3 / 65 (4.62%)	1 / 277 (0.36%)
occurrences (all)	0	3	1
Hyperglycaemia			
subjects affected / exposed	7 / 279 (2.51%)	2 / 65 (3.08%)	8 / 277 (2.89%)
occurrences (all)	9	2	10

Non-serious adverse events	Osimertinib 80 mg (China Cohort)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	69 / 71 (97.18%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Hypertension			
subjects affected / exposed	4 / 71 (5.63%)		
occurrences (all)	5		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	7 / 71 (9.86%)		
occurrences (all)	9		
Pyrexia			
subjects affected / exposed	2 / 71 (2.82%)		
occurrences (all)	2		
Oedema peripheral			
subjects affected / exposed	3 / 71 (4.23%)		
occurrences (all)	4		
Asthenia			
subjects affected / exposed	5 / 71 (7.04%)		
occurrences (all)	5		
Chest discomfort			

subjects affected / exposed	6 / 71 (8.45%)		
occurrences (all)	7		
Non-cardiac chest pain			
subjects affected / exposed	8 / 71 (11.27%)		
occurrences (all)	12		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	14 / 71 (19.72%)		
occurrences (all)	21		
Dyspnoea			
subjects affected / exposed	10 / 71 (14.08%)		
occurrences (all)	12		
Epistaxis			
subjects affected / exposed	3 / 71 (4.23%)		
occurrences (all)	8		
Haemoptysis			
subjects affected / exposed	3 / 71 (4.23%)		
occurrences (all)	3		
Pleural effusion			
subjects affected / exposed	6 / 71 (8.45%)		
occurrences (all)	6		
Productive cough			
subjects affected / exposed	5 / 71 (7.04%)		
occurrences (all)	7		
Oropharyngeal pain			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	6 / 71 (8.45%)		
occurrences (all)	8		
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	11 / 71 (15.49%)		
occurrences (all)	15		
Alanine aminotransferase increased			

subjects affected / exposed	6 / 71 (8.45%)			
occurrences (all)	7			
Electrocardiogram QT prolonged				
subjects affected / exposed	6 / 71 (8.45%)			
occurrences (all)	11			
Weight decreased				
subjects affected / exposed	17 / 71 (23.94%)			
occurrences (all)	23			
White blood cell count decreased				
subjects affected / exposed	29 / 71 (40.85%)			
occurrences (all)	70			
Blood alkaline phosphatase increased				
subjects affected / exposed	6 / 71 (8.45%)			
occurrences (all)	6			
Platelet count decreased				
subjects affected / exposed	20 / 71 (28.17%)			
occurrences (all)	31			
Neutrophil count decreased				
subjects affected / exposed	17 / 71 (23.94%)			
occurrences (all)	35			
Lymphocyte count decreased				
subjects affected / exposed	11 / 71 (15.49%)			
occurrences (all)	14			
Gamma-glutamyltransferase increased				
subjects affected / exposed	6 / 71 (8.45%)			
occurrences (all)	7			
Blood bilirubin increased				
subjects affected / exposed	2 / 71 (2.82%)			
occurrences (all)	3			
Blood albumin decreased				
subjects affected / exposed	5 / 71 (7.04%)			
occurrences (all)	9			
Blood creatinine increased				
subjects affected / exposed	5 / 71 (7.04%)			
occurrences (all)	7			

Blood lactate dehydrogenase increased			
subjects affected / exposed	5 / 71 (7.04%)		
occurrences (all)	5		
Haemoglobin decreased			
subjects affected / exposed	2 / 71 (2.82%)		
occurrences (all)	2		
Blood uric acid increased			
subjects affected / exposed	4 / 71 (5.63%)		
occurrences (all)	7		
Injury, poisoning and procedural complications			
Injury, poisoning and procedural complications			
subjects affected / exposed	3 / 71 (4.23%)		
occurrences (all)	3		
Cardiac disorders			
Left ventricular dysfunction			
subjects affected / exposed	2 / 71 (2.82%)		
occurrences (all)	2		
Nervous system disorders			
Headache			
subjects affected / exposed	7 / 71 (9.86%)		
occurrences (all)	7		
Dysgeusia			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Dizziness			
subjects affected / exposed	3 / 71 (4.23%)		
occurrences (all)	3		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	27 / 71 (38.03%)		
occurrences (all)	38		
Thrombocytopenia			
subjects affected / exposed	7 / 71 (9.86%)		
occurrences (all)	11		
Leukopenia			

subjects affected / exposed	12 / 71 (16.90%)		
occurrences (all)	27		
Neutropenia			
subjects affected / exposed	12 / 71 (16.90%)		
occurrences (all)	24		
Bone marrow failure			
subjects affected / exposed	4 / 71 (5.63%)		
occurrences (all)	13		
Ear and labyrinth disorders			
Ear and labyrinth disorders			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Eye disorders			
Dry eye			
subjects affected / exposed	2 / 71 (2.82%)		
occurrences (all)	4		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	17 / 71 (23.94%)		
occurrences (all)	32		
Stomatitis			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	6		
Nausea			
subjects affected / exposed	10 / 71 (14.08%)		
occurrences (all)	13		
Constipation			
subjects affected / exposed	4 / 71 (5.63%)		
occurrences (all)	5		
Vomiting			
subjects affected / exposed	10 / 71 (14.08%)		
occurrences (all)	12		
Dry mouth			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Abdominal pain			

subjects affected / exposed	2 / 71 (2.82%)		
occurrences (all)	2		
Mouth ulceration			
subjects affected / exposed	12 / 71 (16.90%)		
occurrences (all)	20		
Toothache			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Abdominal pain upper			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Dyspepsia			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	2 / 71 (2.82%)		
occurrences (all)	3		
Drug-induced liver injury			
subjects affected / exposed	2 / 71 (2.82%)		
occurrences (all)	3		
Skin and subcutaneous tissue disorders			
Dermatitis acneiform			
subjects affected / exposed	14 / 71 (19.72%)		
occurrences (all)	15		
Dry skin			
subjects affected / exposed	4 / 71 (5.63%)		
occurrences (all)	4		
Pruritus			
subjects affected / exposed	5 / 71 (7.04%)		
occurrences (all)	6		
Alopecia			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Skin fissures			

subjects affected / exposed	3 / 71 (4.23%)		
occurrences (all)	3		
Rash			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Rash macular			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Rash papular			
subjects affected / exposed	4 / 71 (5.63%)		
occurrences (all)	4		
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	5 / 71 (7.04%)		
occurrences (all)	9		
Rash maculo-papular			
subjects affected / exposed	10 / 71 (14.08%)		
occurrences (all)	10		
Erythema			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Onychoclasis			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	9 / 71 (12.68%)		
occurrences (all)	11		
Haematuria			
subjects affected / exposed	8 / 71 (11.27%)		
occurrences (all)	22		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	7 / 71 (9.86%)		
occurrences (all)	8		
Arthralgia			

subjects affected / exposed	3 / 71 (4.23%)		
occurrences (all)	3		
Musculoskeletal pain			
subjects affected / exposed	4 / 71 (5.63%)		
occurrences (all)	5		
Myalgia			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Muscle spasms			
subjects affected / exposed	3 / 71 (4.23%)		
occurrences (all)	4		
Pain in extremity			
subjects affected / exposed	7 / 71 (9.86%)		
occurrences (all)	7		
Musculoskeletal chest pain			
subjects affected / exposed	2 / 71 (2.82%)		
occurrences (all)	2		
Infections and infestations			
Paronychia			
subjects affected / exposed	9 / 71 (12.68%)		
occurrences (all)	24		
Upper respiratory tract infection			
subjects affected / exposed	9 / 71 (12.68%)		
occurrences (all)	12		
Conjunctivitis			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	2		
Pneumonia			
subjects affected / exposed	2 / 71 (2.82%)		
occurrences (all)	2		
Urinary tract infection			
subjects affected / exposed	8 / 71 (11.27%)		
occurrences (all)	14		
Urinary tract infection bacterial			
subjects affected / exposed	5 / 71 (7.04%)		
occurrences (all)	6		

Influenza subjects affected / exposed occurrences (all)	3 / 71 (4.23%) 3		
Lung infection subjects affected / exposed occurrences (all)	2 / 71 (2.82%) 2		
Nasopharyngitis subjects affected / exposed occurrences (all)	6 / 71 (8.45%) 16		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	10 / 71 (14.08%) 12		
Hypokalaemia subjects affected / exposed occurrences (all)	12 / 71 (16.90%) 18		
Hypoalbuminaemia subjects affected / exposed occurrences (all)	12 / 71 (16.90%) 21		
Hypocalcaemia subjects affected / exposed occurrences (all)	7 / 71 (9.86%) 9		
Hyponatraemia subjects affected / exposed occurrences (all)	9 / 71 (12.68%) 14		
Hypoproteinaemia subjects affected / exposed occurrences (all)	5 / 71 (7.04%) 10		
Hyperglycaemia subjects affected / exposed occurrences (all)	4 / 71 (5.63%) 4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 March 2018	Amendment 3: - The length of time for male and female patients that reliable methods of contraception should be used after discontinuation of study treatment, - QTc interval prolongation with signs and symptoms of serious arrhythmia, and AEs of CTCAE grade 3, - Procedures prior to primary PFS analysis for cross-over patients were clarified, -new text was added to provide guidance on patient procedures after primary PFS analysis and up to final OS analysis; -Changes to the protocol and informed consent form section updated to outline the new process for changes to the CSP, -Removal of template guidance text for Japan that was not removed prior to finalization of the clinical study protocol.

Notes:

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.

There were 19 Chinese subjects who were included in both the global and China cohort which gives a total of 692 participants instead of a total of 673 subjects.

Notes: