Clinical trial results:
A Phase II, Open Label, Single-arm Study to Assess the Safety and Efficacy of AZD9291 in Patients with Locally Advanced/Metastatic Non Small Cell Lung Cancer whose Disease has Progressed with Previous Epidermal Growth Factor Receptor Tyrosine Kinase Inhibitor Therapy and whose Tumours are Epidermal Growth Factor Receptor Mutation and T790M Mutation Positive (AURA2)

Summary

EudraCT number	2014-000531-17
Trial protocol	IT ES
Global end of trial date	07 November 2023

Results information

Result version number	v1 (current)
This version publication date	21 November 2024
First version publication date	21 November 2024

Trial information

Trial identification

Sponsor protocol code	D5160C00002

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	AstraZeneca
Sponsor organisation address	Melbourn Science Park, Cambridge Road, Melbourn, United Kingdom, SG8 6EE
Public contact	Senior Medical Director, Tagrisso, AstraZeneca, ClinicalTrialTransparency@astrazeneca.com
Scientific contact	Senior Medical Director, Tagrisso, AstraZeneca, 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	01 May 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	07 November 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of AZD9291 by assessment of Objective Response Rate (ORR).

Protection of trial subjects:

The study was performed in accordance with ethical principles that have their origin in the Declaration of Helsinki and are consistent with International Conference on Harmonisation / Good Clinical Practice, applicable regulatory requirements and the AstraZeneca policy on Bioethics and Human Biological Samples.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 June 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 35
Country: Number of subjects enrolled	Taiwan: 34
Country: Number of subjects enrolled	Korea, Republic of: 25
Country: Number of subjects enrolled	Japan: 46
Country: Number of subjects enrolled	Italy: 16
Country: Number of subjects enrolled	Hong Kong: 4
Country: Number of subjects enrolled	Spain: 18
Country: Number of subjects enrolled	Canada: 32
Worldwide total number of subjects	210
EEA total number of subjects	34

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)	108
From 65 to 84 years	100
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

First patient enrolled: 28 April 2014, Data cut off: 1 May 2018. The study was open for enrolment at 44 study centres in Canada (3), Hong Kong (2), Italy (5), Japan (14), South Korea (3), Spain (6), Taiwan (2), and the USA (9). This is the final analysis of the study.

Pre-assignment

Screening details:

210 patients were enrolled and received treatment.

Period 1

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

Arms

Arm title	AZD9291 80mg

Arm description:

Daily single dose of AZD9291 80mg

Arm type	Experimental
Investigational medicinal product name	TAGRISSO
Investigational medicinal product code	AZD9291
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

80mg oral

Number of subjects in period 1	AZD9291 80mg
Started	210
Completed	0
Not completed	210
Consent withdrawn by subject	21
Terminated at study close-out	51
Death	134
Not specified	4

Baseline characteristics

Reporting groups	
Reporting group title	AZD9291 80mg
Reporting group description:	
Daily single dose of AZD9291 80mg	

Reporting group values	AZD9291 80mg	Total	
Number of subjects	210	210	
Age, Customized Units: Subjects			
<50 Years|	20	20	
>=50-<65 Years|	88	88	
>=65-<75 Years|	69	69	
>=75 Years|	33	33	
Age Continuous Units: Years			
arithmetic mean	62.9		
standard deviation	± 10.91	-	
Gender, Male/Female Units: Subjects			
Female	145	145	
Male	65	65	
Race, Customized Units: Subjects			
Asian|	132	132	
Black Or African American|	3	3	
Native Hawaiian Or Other Pacific Islander|	1	1	
Other|	2	2	
White|	72	72	

End points

End points reporting groups

Reporting group title	AZD9291 80mg
Reporting group description:	
Daily single dose of AZD9291 80mg	

Primary: Objective Response Rate (ORR)

End point title	Objective Response Rate (ORR)[1]
End point description:	
Per Response Evaluation Criteria in Solid Tumours (RECIST v1.1) assessed by MRI or CT: Complete Response (CR): Disappearance of all target and non-target lesions and no new lesions; Partial Response (PR): >= 30% decrease in the sum of diameters of Target Lesions (compared to baseline) and no new lesions. ORR is the percentage of patients with at least 1 visit response of CR or PR (according to independent review) that was confirmed at least 4 weeks later, prior to progression or further anti-cancer therapy.	
End point type	Primary
End point timeframe:	
RECIST tumour assessments every 6 weeks from first dose until objective disease progression, up to approximately 11 months (at the time of analysis)	
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 performed	

End point values	AZD9291 80mg			
Subject group type	Reporting group			
Number of subjects analysed	200			
Units: % of participants				
number (confidence interval 95%)	70.5 (63.66 to 76.72)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)
End point description:	
OS is the time from date of first dose until death (by any cause) regardless of whether the patient withdrew from AZD9291 therapy. Patients who had not died at the time of analysis were censored at the time of the last date known to be alive.	
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 up to approximately 45 months.	

End point values	AZD9291 80mg			
Subject group type	Reporting group			
Number of subjects analysed	210			
Units: months				
median (confidence interval 95%)	28.3 (24.87 to 31.70)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival (PFS)

End point title	Progression-Free Survival (PFS)

End point description:

Per Response Evaluation Criteria in Solid Tumours (RECIST v1.1) assessed by MRI or CT: Progressive Disease (PD): >= 20% increase in the sum of diameters of TLs and an absolute increase in sum of diameters of >=5mm (compared to the previous minimum sum) or progression of NTLs or a new lesion. PFS is the time from date of first dose until the date of PD (by independent review) or death (by any cause in the absence of progression) regardless of whether the patient withdrew from AZD9291 therapy or received another anti-cancer therapy prior to progression. Patients who had not progressed or died at the time of analysis were censored at the time of the latest date of assessment from their last evaluable RECIST 1.1 assessment.

End point type	Secondary

End point timeframe:

RECIST tumour assessments every 6 weeks from first dose until objective disease progression, up to approximately 11 months (at the time of analysis)

End point values	AZD9291 80mg			
Subject group type	Reporting group			
Number of subjects analysed	210			
Units: months				
median (confidence interval 95%)	9.8 (8.34 to 12.25)			

Statistical analyses

No statistical analyses for this end point

Secondary: Disease Control Rate (DCR)

End point title	Disease Control Rate (DCR)

End point description:

Per Response Evaluation Criteria in Solid Tumours (RECIST v1.1) assessed by MRI or CT: Complete Response (CR): Disappearance of all target and non-target lesions and no new lesions; Partial Response (PR): >= 30% decrease in the sum of diameters of Target Lesions (compared to baseline) and no new lesions; Stable disease (SD): Neither sufficient shrinkage to qualify as a response nor sufficient growth to qualify as progression; Progressive Disease (PD): >= 20% increase in the sum of diameters of TLs and an absolute increase in sum of diameters of >=5mm (compared to the previous minimum sum) or progression of NTLs or a new lesion. DCR is the percentage of patients with best response of CR, PR or SD greater than or equal to 6 weeks (according to independent review), prior to progression (PD) or further anti-cancer therapy.

End point type	Secondary

End point timeframe:

RECIST tumour assessments every 6 weeks from first dose until objective disease progression, up to approximately 11 months (at the time of analysis)

End point values	AZD9291 80mg			
Subject group type	Reporting group			
Number of subjects analysed	200			
Units: % of participants				
number (confidence interval 95%)	91.0 (86.15 to 94.58)			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DoR)

End point title	Duration of Response (DoR)

End point description:

Per Response Evaluation Criteria in Solid Tumours (RECIST v1.1) assessed by MRI or CT: Complete Response (CR): Disappearance of all target and non-target lesions and no new lesions; Partial Response (PR): >= 30% decrease in the sum of diameters of Target Lesions (compared to baseline) and no new lesions. DoR was defined as the time from the date of first documented response (CR or PR that was subsequently confirmed) until the date of documented progression (PD) or death in the absence of disease progression (by independent review).

End point type	Secondary

End point timeframe:

RECIST tumour assessments every 6 weeks from first dose until objective disease progression, up to approximately 11 months (at the time of analysis)

End point values	AZD9291 80mg			
Subject group type	Reporting group			
Number of subjects analysed	141			
Units: months				
median (confidence interval 95%)	11.8 (9.0 to 13.8)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
AEs from start of study drug until 28 days post treatment discontinuation, up to DCO	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups	
Reporting group title	AZD9291 80mg
Reporting group description:	
Daily single dose of AZD9291 80mg	

Serious adverse events	AZD9291 80mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	77 / 210 (36.67%)		
number of deaths (all causes)	136		
number of deaths resulting from adverse events	13		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Myelodysplastic syndrome			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Malignant melanoma			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	3 / 210 (1.43%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Death			

subjects affected / exposed	1 / 210 (0.48%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Pyrexia				
subjects affected / exposed	1 / 210 (0.48%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Fatigue				
subjects affected / exposed	1 / 210 (0.48%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Pulmonary embolism				
subjects affected / exposed	11 / 210 (5.24%)			
occurrences causally related to treatment / all	1 / 14			
deaths causally related to treatment / all	0 / 0			
Pneumonia aspiration				
subjects affected / exposed	1 / 210 (0.48%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Pleurisy				
subjects affected / exposed	1 / 210 (0.48%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pleural effusion				
subjects affected / exposed	1 / 210 (0.48%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Interstitial lung disease				
subjects affected / exposed	2 / 210 (0.95%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	1 / 1			
Dyspnoea				

subjects affected / exposed	3 / 210 (1.43%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
Acute respiratory failure			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonitis			
subjects affected / exposed	3 / 210 (1.43%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Confusional state			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Neutrophil count decreased			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood bilirubin increased			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Radiation necrosis			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Radius fracture				
subjects affected / exposed	1 / 210 (0.48%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Cardio-respiratory arrest				
subjects affected / exposed	1 / 210 (0.48%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Supraventricular tachycardia				
subjects affected / exposed	3 / 210 (1.43%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Syncope				
subjects affected / exposed	2 / 210 (0.95%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Cerebral haemorrhage				
subjects affected / exposed	1 / 210 (0.48%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Brain oedema				
subjects affected / exposed	1 / 210 (0.48%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Altered state of consciousness				
subjects affected / exposed	1 / 210 (0.48%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Transient ischaemic attack				
subjects affected / exposed	1 / 210 (0.48%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			

Thrombotic stroke			
subjects affected / exposed	2 / 210 (0.95%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Headache			
subjects affected / exposed	2 / 210 (0.95%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Cognitive disorder			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cerebral infarction			
subjects affected / exposed	2 / 210 (0.95%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			

subjects affected / exposed	3 / 210 (1.43%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Small intestinal obstruction				
subjects affected / exposed	2 / 210 (0.95%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Rectal haemorrhage				
subjects affected / exposed	1 / 210 (0.48%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Large intestine polyp				
subjects affected / exposed	1 / 210 (0.48%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastritis				
subjects affected / exposed	1 / 210 (0.48%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Jaundice				
subjects affected / exposed	1 / 210 (0.48%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatitis fulminant				
subjects affected / exposed	1 / 210 (0.48%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Drug-induced liver injury				
subjects affected / exposed	1 / 210 (0.48%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				

Lichen sclerosus			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Pathological fracture			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Osteoporotic fracture			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal pain			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bone pain			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Back pain			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Clostridium difficile colitis			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Urinary tract infection				
subjects affected / exposed	1 / 210 (0.48%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Upper respiratory tract infection				
subjects affected / exposed	1 / 210 (0.48%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	2 / 210 (0.95%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Respiratory tract infection bacterial				
subjects affected / exposed	1 / 210 (0.48%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Respiratory tract infection				
subjects affected / exposed	2 / 210 (0.95%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Pneumonia bacterial				
subjects affected / exposed	2 / 210 (0.95%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Pneumonia				
subjects affected / exposed	7 / 210 (3.33%)			
occurrences causally related to treatment / all	0 / 8			
deaths causally related to treatment / all	0 / 3			
Pharyngeal abscess				
subjects affected / exposed	1 / 210 (0.48%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Lung infection				

subjects affected / exposed	2 / 210 (0.95%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Influenza			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	2 / 210 (0.95%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Failure to thrive			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Dehydration			
subjects affected / exposed	1 / 210 (0.48%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	AZD9291 80mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	200 / 210 (95.24%)		
Investigations			
Weight decreased			
subjects affected / exposed	15 / 210 (7.14%)		
occurrences (all)	18		
Aspartate aminotransferase increased			
subjects affected / exposed	26 / 210 (12.38%)		
occurrences (all)	28		
Alanine aminotransferase increased			

subjects affected / exposed occurrences (all)	25 / 210 (11.90%) 31		
Blood creatinine increased subjects affected / exposed occurrences (all)	11 / 210 (5.24%) 14		
White blood cell count decreased subjects affected / exposed occurrences (all)	22 / 210 (10.48%) 39		
Platelet count decreased subjects affected / exposed occurrences (all)	25 / 210 (11.90%) 34		
Neutrophil count decreased subjects affected / exposed occurrences (all)	18 / 210 (8.57%) 27		
Electrocardiogram qt prolonged subjects affected / exposed occurrences (all)	14 / 210 (6.67%) 18		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	19 / 210 (9.05%) 23		
Dysgeusia subjects affected / exposed occurrences (all)	11 / 210 (5.24%) 12		
Headache subjects affected / exposed occurrences (all)	35 / 210 (16.67%) 50		
Blood and lymphatic system disorders Thrombocytopenia subjects affected / exposed occurrences (all)	17 / 210 (8.10%) 26		
Anaemia subjects affected / exposed occurrences (all)	35 / 210 (16.67%) 44		
Neutropenia			

subjects affected / exposed	15 / 210 (7.14%)		
occurrences (all)	28		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	21 / 210 (10.00%)		
occurrences (all)	26		
Oedema peripheral			
subjects affected / exposed	28 / 210 (13.33%)		
occurrences (all)	34		
Fatigue			
subjects affected / exposed	43 / 210 (20.48%)		
occurrences (all)	51		
Asthenia			
subjects affected / exposed	17 / 210 (8.10%)		
occurrences (all)	19		
Eye disorders			
Dry eye			
subjects affected / exposed	14 / 210 (6.67%)		
occurrences (all)	28		
Cataract			
subjects affected / exposed	13 / 210 (6.19%)		
occurrences (all)	13		
Vision blurred			
subjects affected / exposed	13 / 210 (6.19%)		
occurrences (all)	14		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	47 / 210 (22.38%)		
occurrences (all)	59		
Abdominal pain upper			
subjects affected / exposed	15 / 210 (7.14%)		
occurrences (all)	21		
Abdominal pain			
subjects affected / exposed	13 / 210 (6.19%)		
occurrences (all)	16		
Stomatitis			

subjects affected / exposed	33 / 210 (15.71%)		
occurrences (all)	47		
Diarrhoea			
subjects affected / exposed	99 / 210 (47.14%)		
occurrences (all)	155		
Nausea			
subjects affected / exposed	49 / 210 (23.33%)		
occurrences (all)	61		
Vomiting			
subjects affected / exposed	34 / 210 (16.19%)		
occurrences (all)	36		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	44 / 210 (20.95%)		
occurrences (all)	65		
Dyspnoea			
subjects affected / exposed	29 / 210 (13.81%)		
occurrences (all)	33		
Rhinorrhoea			
subjects affected / exposed	17 / 210 (8.10%)		
occurrences (all)	21		
Oropharyngeal pain			
subjects affected / exposed	14 / 210 (6.67%)		
occurrences (all)	15		
Epistaxis			
subjects affected / exposed	13 / 210 (6.19%)		
occurrences (all)	19		
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	24 / 210 (11.43%)		
occurrences (all)	31		
Skin fissures			
subjects affected / exposed	15 / 210 (7.14%)		
occurrences (all)	22		
Rash			

subjects affected / exposed	54 / 210 (25.71%)		
occurrences (all)	68		
Pruritus			
subjects affected / exposed	38 / 210 (18.10%)		
occurrences (all)	47		
Dry skin			
subjects affected / exposed	59 / 210 (28.10%)		
occurrences (all)	68		
Dermatitis acneiform			
subjects affected / exposed	25 / 210 (11.90%)		
occurrences (all)	27		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	20 / 210 (9.52%)		
occurrences (all)	21		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	41 / 210 (19.52%)		
occurrences (all)	54		
Arthralgia			
subjects affected / exposed	28 / 210 (13.33%)		
occurrences (all)	37		
Muscle spasms			
subjects affected / exposed	26 / 210 (12.38%)		
occurrences (all)	27		
Musculoskeletal pain			
subjects affected / exposed	19 / 210 (9.05%)		
occurrences (all)	23		
Neck pain			
subjects affected / exposed	12 / 210 (5.71%)		
occurrences (all)	12		
Pain in extremity			
subjects affected / exposed	25 / 210 (11.90%)		
occurrences (all)	32		
Musculoskeletal chest pain			

subjects affected / exposed occurrences (all)	21 / 210 (10.00%) 24		
Infections and infestations Urinary tract infection subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all) Paronychia subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all)	 22 / 210 (10.48%) 27 26 / 210 (12.38%) 43 45 / 210 (21.43%) 53 35 / 210 (16.67%) 53		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	 51 / 210 (24.29%) 66		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

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.

Of the efficacy data, only the OS data was re-analysed at this final cut-off (data cut-off 01MAY2018). No formal statistical analyses were performed as this is a single-arm study.

Notes: