Clinical trial results:
A Phase III/IV, Single Arm, Multicenter Study of Atezolizumab (Tecentriq) to Investigate Long-term Safety and Efficacy in Previously-treated Patients with Locally Advanced or Metastatic Non-small Cell Lung Cancer (TAIL)

Summary

EudraCT number	2017-001409-34
Trial protocol	SI SE DK LV PL GB NL ES GR IT
Global end of trial date	07 April 2022

Results information

Result version number	v2
This version publication date	09 February 2024
First version publication date	31 March 2023
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	MO39171

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03285763
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.com
Scientific contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.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	07 April 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	07 April 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this trial was to evaluate the long-term safety and efficacy of atezolizumab treatment in participants with Stage IIIb or Stage IV Non-small Cell Lung Cancer (NSCLC) who had progressed after standard systemic chemotherapy (including if given in combination with anti-programmed cell death protein 1 [anti-PD-1] therapy, after anti-PD-1 as monotherapy, or after tyrosine kinase inhibitor [TKI] therapy).

Protection of trial subjects:

All study subjects were required to read and sign and Informed Consent Form.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 October 2017
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	30 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 8
Country: Number of subjects enrolled	Brazil: 22
Country: Number of subjects enrolled	China: 30
Country: Number of subjects enrolled	Colombia: 3
Country: Number of subjects enrolled	Costa Rica: 5
Country: Number of subjects enrolled	Denmark: 15
Country: Number of subjects enrolled	Greece: 40
Country: Number of subjects enrolled	Guatemala: 3
Country: Number of subjects enrolled	Italy: 78
Country: Number of subjects enrolled	Latvia: 10
Country: Number of subjects enrolled	Lebanon: 10
Country: Number of subjects enrolled	Malaysia: 30
Country: Number of subjects enrolled	Mexico: 39
Country: Number of subjects enrolled	Morocco: 5
Country: Number of subjects enrolled	Netherlands: 30
Country: Number of subjects enrolled	Panama: 3
Country: Number of subjects enrolled	Peru: 7

Country: Number of subjects enrolled	Philippines: 10
Country: Number of subjects enrolled	Poland: 51
Country: Number of subjects enrolled	Slovenia: 4
Country: Number of subjects enrolled	Spain: 159
Country: Number of subjects enrolled	Sweden: 19
Country: Number of subjects enrolled	United Arab Emirates: 1
Country: Number of subjects enrolled	United Kingdom: 33
Worldwide total number of subjects	615
EEA total number of subjects	406

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)	308
From 65 to 84 years	303
85 years and over	4

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at 111 sites across 24 countries.

Pre-assignment

Screening details:

Four enrolled participants died without receiving study 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	Atezolizumab

Arm description:

Participants with Stage IIIb or State IV NSCLC who had progressed after standard systemic chemotherapy received atezolizumab until Investigator-assessed loss of clinical benefit, unacceptable toxicity, investigator or participant's decision to withdraw from therapy, or death (whichever occurred first).

Arm type	Experimental
Investigational medicinal product name	Atezolizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received 1200 milligrams (mg) of atezolizumab administered by intravenous infusion on Day 1 of every 3-week cycle until Investigator-assessed loss of clinical benefit, unacceptable toxicity, investigator or participant's decision to withdraw from therapy, or death (whichever occurred first).

Number of subjects in period 1	Atezolizumab
Started	615
Completed	13
Not completed	602
Physician decision	2
Consent withdrawn by subject	33
Study Terminated By Sponsor	79
Death	470
Lost to follow-up	18

Baseline characteristics

Reporting groups	
Reporting group title	Atezolizumab
Reporting group description:	
Participants with Stage IIIb or State IV NSCLC who had progressed after standard systemic chemotherapy received atezolizumab until Investigator-assessed loss of clinical benefit, unacceptable toxicity, investigator or participant's decision to withdraw from therapy, or death (whichever occurred first).	

Reporting group values	Atezolizumab	Total	
Number of subjects	615	615	
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)	308	308	
From 65-84 years	303	303	
85 years and over	4	4	
Age Continuous Units: years			
arithmetic mean	63.7		
standard deviation	± 9.9	-	
Gender Categorical Units: Participants			
Female	245	245	
Male	370	370	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	93	93	
Not Hispanic or Latino	509	509	
Unknown or Not Reported	13	13	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	44	44	
Asian	76	76	
Native Hawaiian or Other Pacific Islander	1	1	
Black or African American	4	4	
White	483	483	
More than one race	5	5	
Unknown or Not Reported	2	2	
Region Units: Subjects			

EMEA (Europe, the Middle East, and Africa)	455	455	
Asia	70	70	
LATAM (Latin America)	90	90	
ECOG Performance Status			
ECOG Performance Status is graded from 0-5 with a lower number representing no or limited impact on daily living activities and a higher number represents greater impact on daily living activities. ECOG performance status 0 (fully active), ECOG performance status 1 (restricted in physically strenuous activity), ECOG performance status 2 (ambulatory and capable of selfcare; unable to carry out work activities).			
Units: Subjects			
ECOG performance status 0	193	193	
ECOG performance status 1	361	361	
ECOG performance status 2	61	61	
Smoking Status Units: Subjects			
Never	127	127	
Current	115	115	
Previous	373	373	
eGFR (mL/min/1.73 m^2) at baseline Units: Subjects			
15-<30	2	2	
30-<60	77	77	
60-<90	251	251	
>=90	283	283	
Missing	2	2	

End points

End points reporting groups

Reporting group title	Atezolizumab

Reporting group description:

Participants with Stage IIIb or State IV NSCLC who had progressed after standard systemic chemotherapy received atezolizumab until Investigator-assessed loss of clinical benefit, unacceptable toxicity, investigator or participant's decision to withdraw from therapy, or death (whichever occurred first).

Primary: Percentage of Participants with Adverse Events

End point title	Percentage of Participants with Adverse Events[1]

End point description:

An adverse event (AE) was defined as any untoward medical occurrence in a participant administered a pharmaceutical product, regardless of causal attribution. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom or disease temporally associated with the use of a pharmaceutical product whether or not considered related to the pharmaceutical product. Preexisting conditions which worsen during a study are also considered as a AEs. The safety population was based on all participants who received any dose of atezolizumab during the study treatment.

End point type	Primary

End point timeframe:

Baseline up to 4 years

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 were conducted.

End point values	Atezolizumab			
Subject group type	Reporting group			
Number of subjects analysed	615			
Units: Percentage of Participants				
number (not applicable)	91.7			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival (PFS) Based on Disease Status as Evaluated By the Investigator in Accordance With Response Evaluation Criteria in Solid Tumors (RECIST), Version 1.1 (v.1.1)

End point title	Progression-Free Survival (PFS) Based on Disease Status as Evaluated By the Investigator in Accordance With Response Evaluation Criteria in Solid Tumors (RECIST), Version 1.1 (v.1.1)

End point description:

PFS according to RECIST 1.1 was defined as the time (in months) from initiation of study treatment to the first documented disease progression as determined by the investigator per RECIST 1.1, or death from any cause, whichever occurred first. The safety population was based on all participants who received any dose of atezolizumab during the study treatment. This was a single-arm study. The study population was participants with Stage IIIB or Stage IV NSCLC. The primary objective of this study was

to understand the safety in this participant population (without distinction of Stage IIIB and IV) and it was not planned to analyze them separately as per the protocol.

End point type	Secondary

End point timeframe:

Baseline up to disease progression or death whichever occurs first (up to 4 years)

End point values	Atezolizumab			
Subject group type	Reporting group			
Number of subjects analysed	615			
Units: Months				
median (confidence interval 95%)	2.7 (2.3 to 2.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Alive 2 Years After Initiation of Treatment

End point title	Percentage of Participants Alive 2 Years After Initiation of Treatment

End point description:

The overall survival (OS) rate at 2 years, was defined as the percentage of participants remaining alive 2 years after initiation of study treatment. The safety population was based on all participants who received any dose of atezolizumab during the study treatment.

End point type	Secondary

End point timeframe:

Baseline up to Year 2

End point values	Atezolizumab			
Subject group type	Reporting group			
Number of subjects analysed	615			
Units: Percentage of Participants				
number (not applicable)	26.7			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

OS was defined as the time (in months) from initiation of study treatment to death from any cause. The safety population was based on all participants who received any dose of atezolizumab during the study

treatment.

End point type	Secondary

End point timeframe:

Baseline up to death (up to 4 years)

End point values	Atezolizumab			
Subject group type	Reporting group			
Number of subjects analysed	615			
Units: Months				
median (confidence interval 95%)	11.2 (8.9 to 12.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: EuroQol 5-Dimension 5-Level (EQ-5D-5L) Questionnaire

End point title	EuroQol 5-Dimension 5-Level (EQ-5D-5L) Questionnaire

End point description:

The EQ-5D-5L was a self-reported health status questionnaire that consisted of six questions used to calculate a health utility score for use in health economic analysis. The EQ-5D-5L has two components: a five-item health state profile that assesses mobility, self-care, usual activities, pain/discomfort, and anxiety/depression, as well as a visual analog scale (VAS) that measures health state. Overall scores range from 0 to 1, with low scores representing a higher level of dysfunction. The safety population was based on all participants who received any dose of atezolizumab during the study treatment. EQ-5D-5L was planned to be utilized for economic modeling only outside of the statistical analysis plan. There is no data to report.

End point type	Secondary

End point timeframe:

Day 1 of first 3 cycles (21-day cycle), then every 6 weeks for 48 weeks; thereafter every 9 weeks until disease progression or until treatment discontinuation (up to 4 years)

End point values	Atezolizumab			
Subject group type	Reporting group			
Number of subjects analysed	0[2]			
Units: Percentage of Participants				
number (not applicable)				

Notes:

[2] - EQ-5D-5L was planned to be utilized for economic modeling outside of the statistical analysis plan.

Statistical analyses

No statistical analyses for this end point

Secondary: European Organisation for Research and Treatment of Cancer Quality-of-

Life Questionnaire Supplemental Lung Cancer Module (EORTC QLQ-LC13)

End point title	European Organisation for Research and Treatment of Cancer Quality-of-Life Questionnaire Supplemental Lung Cancer Module (EORTC QLQ-LC13)

End point description:

The EORTC QLQ-LC13 consisted of 13 items that address key lung cancer symptoms (cough, hemoptysis, dyspnea, and site-specific pain), treatment-related adverse effects (sore mouth, dysphagia, peripheral neuropathy and alopecia) and pain medication. The dysphagia scale is multi-item, while the rest are single-item scales. The scales are linearly transformed so that each score has a range from 0 to 100. A high scale score represents a higher response level (e.g. a high score for global health status represents a high QoL). A high score for the symptom scale represents a high level of symptoms. A >=10-point change in the EORTC scale score was perceived by participants as clinically significant. Values presented after baseline represent the change from baseline.
The safety population was based on all participants who received any dose of atezolizumab during the study treatment. 9999999 = no data. Values presented after baseline represent the change from baseline.

End point type	Secondary

End point timeframe:

Day 1 of first 3 cycles (21-day cycle), then every 6 weeks for 48 weeks; thereafter every 9 weeks until disease progression or until treatment discontinuation (up to 4 years)

End point values	Atezolizumab			
Subject group type	Reporting group			
Number of subjects analysed	615			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Dyspnoea: Baseline	24.82 (± 21.64)			
Dyspnoea: Cycle (C) 02 Day (D) 01	2.41 (± 15.59)			
Dyspnoea: Tumor Assessment Wk 006	1.59 (± 18.91)			
Dyspnoea: Tumor Assessment Wk 012	-0.62 (± 19.40)			
Dyspnoea: Tumor Assessment Wk 018	-0.50 (± 17.91)			
Dyspnoea: Tumor Assessment Wk 024	-2.84 (± 17.90)			
Dyspnoea: Tumor Assessment Wk 030	-1.17 (± 21.29)			
Dyspnoea: Tumor Assessment Wk 036	-3.91 (± 20.51)			
Dyspnoea: Tumor Assessment Wk 042	-3.97 (± 19.10)			
Dyspnoea: Tumor Assessment Wk 048	-3.65 (± 20.44)			
Dyspnoea: Tumor Assessment Wk 054	2.38 (± 16.98)			
Dyspnoea: Tumor Assessment Wk 057	-5.25 (± 18.13)			
Dyspnoea: Tumor Assessment Wk 060	-1.11 (± 11.05)			
Dyspnoea: Tumor Assessment Wk 066	1.09 (± 19.53)			
Dyspnoea: Tumor Assessment Wk 072	4.76 (± 30.67)			
Dyspnoea: Tumor Assessment Wk 075	-2.22 (± 18.52)			
Dyspnoea: Tumor Assessment Wk 078	0.00 (± 42.31)			
Dyspnoea: Tumor Assessment Wk 084	-2.92 (± 16.07)			

Dyspnoea: Tumor Assessment Wk 090	-17.78 (± 12.67)			
Dyspnoea: Tumor Assessment Wk 093	-3.57 (± 19.38)			
Dyspnoea: Tumor Assessment Wk 096	13.33 (± 27.67)			
Dyspnoea: Tumor Assessment Wk 102	-5.95 (± 19.24)			
Dyspnoea: Tumor Assessment Wk 108	-8.89 (± 26.53)			
Dyspnoea: Tumor Assessment Wk 111	-6.88 (± 17.02)			
Dyspnoea: Tumor Assessment Wk 114	-16.67 (± 23.57)			
Dyspnoea: Tumor Assessment Wk 120	-5.85 (± 14.04)			
Dyspnoea: Tumor Assessment Wk 126	-18.52 (± 27.96)			
Dyspnoea: Tumor Assessment Wk 129	-7.19 (± 13.57)			
Dyspnoea: Tumor Assessment Wk 132	-22.22 (± 9999999)			
Dyspnoea: Tumor Assessment Wk 138	-1.71 (± 11.87)			
Dyspnoea: Tumor Assessment Wk 144	0.00 (± 9999999)			
Dyspnoea: Tumor Assessment Wk 147	-3.70 (± 7.86)			
Dyspnoea: Tumor Assessment Wk 156	6.94 (± 23.71)			
Dyspnoea: Tumor Assessment Wk 165	3.70 (± 23.13)			
Dyspnoea: Tumor Assessment Wk 174	0.00 (± 9999999)			
Dyspnoea: Tumor Assessment Wk 183	-11.11 (± 9999999)			
Coughing: Baseline	33.84 (± 25.94)			
Coughing: C2D1	0.80 (± 21.89)			
Coughing: Tumor Assessment Wk 006	-0.68 (± 24.84)			
Coughing: Tumor Assessment Wk 012	-4.44 (± 28.35)			
Coughing: Tumor Assessment Wk 018	-7.88 (± 25.61)			
Coughing: Tumor Assessment Wk 024	-7.83 (± 26.95)			
Coughing: Tumor Assessment Wk 030	-7.18 (± 26.30)			
Coughing: Tumor Assessment Wk 036	-9.32 (± 25.71)			
Coughing: Tumor Assessment Wk 042	-13.18 (± 25.71)			
Coughing: Tumor Assessment Wk 048	-9.26 (± 30.76)			
Coughing: Tumor Assessment Wk 054	-2.38 (± 24.33)			
Coughing: Tumor Assessment Wk 057	-13.22 (± 28.57)			
Coughing: Tumor Assessment Wk 060	-9.09 (± 21.56)			
Coughing: Tumor Assessment Wk 066	-10.69 (± 28.32)			

Coughing: Tumor Assessment Wk 072	-4.76 (± 23.00)			
Coughing: Tumor Assessment Wk 075	-18.33 (± 28.19)			
Coughing: Tumor Assessment Wk 078	0.00 (± 33.33)			
Coughing: Tumor Assessment Wk 084	-16.67 (± 31.72)			
Coughing: Tumor Assessment Wk 090	-16.67 (± 18.26)			
Coughing: Tumor Assessment Wk 093	-16.67 (± 30.77)			
Coughing: Tumor Assessment Wk 096	6.67 (± 14.91)			
Coughing: Tumor Assessment Wk 102	-23.81 (± 25.43)			
Coughing: Tumor Assessment Wk 108	-6.67 (± 27.89)			
Coughing: Tumor Assessment Wk 111	-11.11 (± 30.43)			
Coughing: Tumor Assessment Wk 114	-16.67 (± 23.57)			
Coughing: Tumor Assessment Wk 120	-12.28 (± 29.84)			
Coughing: Tumor Assessment Wk 126	0.00 (± 33.33)			
Coughing: Tumor Assessment Wk 129	-11.76 (± 26.20)			
Coughing: Tumor Assessment Wk 132	0.00 (± 9999999)			
Coughing: Tumor Assessment Wk 138	-14.29 (± 31.25)			
Coughing: Tumor Assessment Wk 144	33.33 (± 9999999)			
Coughing: Tumor Assessment Wk 147	-22.22 (± 40.82)			
Coughing: Tumor Assessment Wk 156	-12.50 (± 53.27)			
Coughing: Tumor Assessment Wk 165	0.00 (± 33.33)			
Coughing: Tumor Assessment Wk 174	33.33 (± 9999999)			
Coughing: Tumor Assessment Wk 183	0.00 (± 9999999)			
Haemoptysis: Baseline	3.02 (± 10.15)			
Haemoptysis: C2D1	0.60 (± 9.05)			
Haemoptysis: Tumor Assessment Wk 006	0.10 (± 9.81)			
Haemoptysis: Tumor Assessment Wk 012	0.15 (± 9.77)			
Haemoptysis: Tumor Assessment Wk 018	-0.18 (± 8.96)			
Haemoptysis: Tumor Assessment Wk 024	-0.67 (± 9.06)			
Haemoptysis: Tumor Assessment Wk 030	-0.29 (± 10.31)			
Haemoptysis: Tumor Assessment Wk 036	-1.79 (± 10.27)			
Haemoptysis: Tumor Assessment Wk 042	0.00 (± 11.43)			
Haemoptysis: Tumor Assessment Wk 048	-0.46 (± 8.83)			
Haemoptysis: Tumor Assessment Wk 054	0.00 (± 13.07)			

Haemoptysis: Tumor Assessment Wk 057	0.00 (± 10.91)			
Haemoptysis: Tumor Assessment Wk 060	0.00 (± 14.91)			
Haemoptysis: Tumor Assessment Wk 066	-2.52 (± 8.89)			
Haemoptysis: Tumor Assessment Wk 072	0.00 (± 0.00)			
Haemoptysis: Tumor Assessment Wk 075	-3.33 (± 10.13)			
Haemoptysis: Tumor Assessment Wk 078	0.00 (± 0.00)			
Haemoptysis: Tumor Assessment Wk 084	-2.63 (± 9.11)			
Haemoptysis: Tumor Assessment Wk 090	5.56 (± 13.61)			
Haemoptysis: Tumor Assessment Wk 093	1.19 (± 14.29)			
Haemoptysis: Tumor Assessment Wk 096	0.00 (± 0.00)			
Haemoptysis: Tumor Assessment Wk 102	-2.38 (± 8.74)			
Haemoptysis: Tumor Assessment Wk 108	0.00 (± 0.00)			
Haemoptysis: Tumor Assessment Wk 111	-3.17 (± 10.03)			
Haemoptysis: Tumor Assessment Wk 114	0.00 (± 0.00)			
Haemoptysis: Tumor Assessment Wk 120	-1.75 (± 13.49)			
Haemoptysis: Tumor Assessment Wk 126	0.00 (± 0.00)			
Haemoptysis: Tumor Assessment Wk 129	-1.96 (± 14.29)			
Haemoptysis: Tumor Assessment Wk 132	0.00 (± 9999999)			
Haemoptysis: Tumor Assessment Wk 138	-2.38 (± 15.82)			
Haemoptysis: Tumor Assessment Wk 144	0.00 (± 9999999)			
Haemoptysis: Tumor Assessment Wk 147	0.00 (± 9999999)			
Haemoptysis: Tumor Assessment Wk 156	0.00 (± 0.00)			
Haemoptysis: Tumor Assessment Wk 165	0.00 (± 33.33)			
Haemoptysis: Tumor Assessment Wk 174	-33.33 (± 9999999)			
Haemoptysis: Tumor Assessment Wk 183	0.00 (± 9999999)			
Sore mouth: Baseline	3.58 (± 12.33)			
Sore mouth: C2D1	0.67 (± 15.76)			
Sore mouth: Tumor Assessment Wk 006	0.49 (± 16.95)			
Sore mouth: Tumor Assessment Wk 012	0.00 (± 16.55)			
Sore mouth: Tumor Assessment Wk 018	-0.73 (± 14.00)			
Sore mouth: Tumor Assessment Wk 024	-1.13 (± 14.24)			
Sore mouth: Tumor Assessment Wk 030	-2.03 (± 14.16)			

Sore mouth: Tumor Assessment Wk 036	-2.54 (± 15.02)			
Sore mouth: Tumor Assessment Wk 042	-1.57 (± 16.99)			
Sore mouth: Tumor Assessment Wk 048	-4.29 (± 15.97)			
Sore mouth: Tumor Assessment Wk 054	2.56 (± 16.45)			
Sore mouth: Tumor Assessment Wk 057	-1.75 (± 11.65)			
Sore mouth: Tumor Assessment Wk 060	-3.33 (± 10.54)			
Sore mouth: Tumor Assessment Wk 066	-2.56 (± 14.53)			
Sore mouth: Tumor Assessment Wk 072	0.00 (± 0.00)			
Sore mouth: Tumor Assessment Wk 075	-2.50 (± 13.89)			
Sore mouth: Tumor Assessment Wk 078	6.67 (± 14.91)			
Sore mouth: Tumor Assessment Wk 084	-1.75 (± 13.30)			
Sore mouth: Tumor Assessment Wk 090	0.00 (± 0.00)			
Sore mouth: Tumor Assessment Wk 093	2.38 (± 8.74)			
Sore mouth: Tumor Assessment Wk 096	0.00 (± 0.00)			
Sore mouth: Tumor Assessment Wk 102	1.19 (± 6.30)			
Sore mouth: Tumor Assessment Wk 108	0.00 (± 0.00)			
Sore mouth: Tumor Assessment Wk 111	3.17 (± 10.03)			
Sore mouth: Tumor Assessment Wk 114	33.33 (± 47.14)			
Sore mouth: Tumor Assessment Wk 120	7.02 (± 17.84)			
Sore mouth: Tumor Assessment Wk 126	11.11 (± 19.25)			
Sore mouth: Tumor Assessment Wk 129	0.00 (± 0.00)			
Sore mouth: Tumor Assessment Wk 132	33.33 (± 9999999)			
Sore mouth: Tumor Assessment Wk 138	2.38 (± 8.91)			
Sore mouth: Tumor Assessment Wk 144	0.00 (± 9999999)			
Sore mouth: Tumor Assessment Wk 147	0.00 (± 0.00)			
Sore mouth: Tumor Assessment Wk 156	0.00 (± 0.00)			
Sore mouth: Tumor Assessment Wk 165	0.00 (± 0.00)			
Sore mouth: Tumor Assessment Wk 174	0.00 (± 9999999)			
Sore mouth: Tumor Assessment Wk 183	0.00 (± 9999999)			
Dysphagia: Baseline	5.46 (± 14.73)			
Dysphagia: C2D1	0.20 (± 13.92)			
Dysphagia: Tumor Assessment Wk 006	-1.38 (± 13.74)			
Dysphagia: Tumor Assessment Wk 012	-0.15 (± 16.63)			
Dysphagia: Tumor Assessment Wk 018	0.74 (± 16.08)			
Dysphagia: Tumor Assessment Wk 024	-1.59 (± 11.26)			
Dysphagia: Tumor Assessment Wk 030	-1.46 (± 10.30)			
Dysphagia: Tumor Assessment Wk 036	-1.83 (± 16.00)			
Dysphagia: Tumor Assessment Wk 042	-1.59 (± 13.60)			

Dysphagia: Tumor Assessment Wk 048	-0.48 (± 15.53)			
Dysphagia: Tumor Assessment Wk 054	-2.56 (± 9.25)			
Dysphagia: Tumor Assessment Wk 057	-0.58 (± 9.94)			
Dysphagia: Tumor Assessment Wk 060	0.00 (± 0.00)			
Dysphagia: Tumor Assessment Wk 066	-1.28 (± 11.36)			
Dysphagia: Tumor Assessment Wk 072	0.00 (± 0.00)			
Dysphagia: Tumor Assessment Wk 075	0.00 (± 15.10)			
Dysphagia: Tumor Assessment Wk 078	0.00 (± 0.00)			
Dysphagia: Tumor Assessment Wk 084	-2.63 (± 11.96)			
Dysphagia: Tumor Assessment Wk 090	0.00 (± 0.00)			
Dysphagia: Tumor Assessment Wk 093	-2.38 (± 8.74)			
Dysphagia: Tumor Assessment Wk 096	6.67 (± 14.91)			
Dysphagia: Tumor Assessment Wk 102	-2.38 (± 8.74)			
Dysphagia: Tumor Assessment Wk 108	0.00 (± 0.00)			
Dysphagia: Tumor Assessment Wk 111	0.00 (± 10.54)			
Dysphagia: Tumor Assessment Wk 114	0.00 (± 0.00)			
Dysphagia: Tumor Assessment Wk 120	-1.75 (± 7.65)			
Dysphagia: Tumor Assessment Wk 126	0.00 (± 0.00)			
Dysphagia: Tumor Assessment Wk 129	0.00 (± 0.00)			
Dysphagia: Tumor Assessment Wk 132	0.00 (± 9999999)			
Dysphagia: Tumor Assessment Wk 138	0.00 (± 0.00)			
Dysphagia: Tumor Assessment Wk 144	0.00 (± 9999999)			
Dysphagia: Tumor Assessment Wk 147	0.00 (± 0.00)			
Dysphagia: Tumor Assessment Wk 156	4.17 (± 11.79)			
Dysphagia: Tumor Assessment Wk 165	0.00 (± 0.00)			
Dysphagia: Tumor Assessment Wk 174	0.00 (± 9999999)			
Dysphagia: Tumor Assessment Wk 183	0.00 (± 9999999)			
Peripheral neuropathy: Baseline	17.77 (± 26.96)			
Peripheral neuropathy: C2D1	-0.20 (± 22.29)			
Peripheral neuropathy: Tumor Assessment Wk 006	-0.58 (± 21.80)			
Peripheral neuropathy: Tumor Assessment Wk 012	0.15 (± 24.20)			
Peripheral neuropathy: Tumor Assessment Wk 018	-2.56 (± 26.56)			
Peripheral neuropathy: Tumor Assessment Wk 024	-3.15 (± 25.30)			
Peripheral neuropathy: Tumor Assessment Wk 030	-3.19 (± 24.17)			
Peripheral neuropathy: Tumor Assessment Wk 036	-6.23 (± 25.29)			
Peripheral neuropathy: Tumor Assessment Wk 042	-7.45 (± 28.35)			
Peripheral neuropathy: Tumor Assessment Wk 048	-8.92 (± 27.58)			
Peripheral neuropathy: Tumor Assessment Wk 054	-7.69 (± 19.97)			
Peripheral neuropathy: Tumor Assessment Wk 057	-6.32 (± 20.19)			

Peripheral neuropathy: Tumor Assessment Wk 060	-13.33 (± 17.21)			
Peripheral neuropathy: Tumor Assessment Wk 066	-3.85 (± 22.53)			
Peripheral neuropathy: Tumor Assessment Wk 072	-4.76 (± 23.00)			
Peripheral neuropathy: Tumor Assessment Wk 075	-10.83 (± 26.57)			
Peripheral neuropathy: Tumor Assessment Wk 078	-6.67 (± 27.89)			
Peripheral neuropathy: Tumor Assessment Wk 084	-9.65 (± 28.90)			
Peripheral neuropathy: Tumor Assessment Wk 090	0.00 (± 21.08)			
Peripheral neuropathy: Tumor Assessment Wk 093	-5.95 (± 30.16)			
Peripheral neuropathy: Tumor Assessment Wk 096	6.67 (± 14.91)			
Peripheral neuropathy: Tumor Assessment Wk 102	-8.33 (± 26.64)			
Peripheral neuropathy: Tumor Assessment Wk 108	-6.67 (± 14.91)			
Peripheral neuropathy: Tumor Assessment Wk 111	-14.29 (± 34.27)			
Peripheral neuropathy: Tumor Assessment Wk 114	-16.67 (± 23.57)			
Peripheral neuropathy: Tumor Assessment Wk 120	-14.04 (± 32.04)			
Peripheral neuropathy: Tumor Assessment Wk 126	-11.11 (± 19.25)			
Peripheral neuropathy: Tumor Assessment Wk 129	-7.84 (± 25.08)			
Peripheral neuropathy: Tumor Assessment Wk 132	0.00 (± 9999999)			
Peripheral neuropathy: Tumor Assessment Wk 138	-19.05 (± 33.88)			
Peripheral neuropathy: Tumor Assessment Wk 144	0.00 (± 9999999)			
Peripheral neuropathy: Tumor Assessment Wk 147	-22.22 (± 40.82)			
Peripheral neuropathy: Tumor Assessment Wk 156	-12.50 (± 50.20)			
Peripheral neuropathy: Tumor Assessment Wk 165	11.11 (± 19.25)			
Peripheral neuropathy: Tumor Assessment Wk 174	33.33 (± 9999999)			
Peripheral neuropathy: Tumor Assessment Wk 183	33.33 (± 9999999)			
Alopecia: Baseline	13.95 (± 27.14)			
Alopecia: C2D1	-5.64 (± 24.32)			
Alopecia: Tumor Assessment Wk 006	-4.31 (± 24.84)			
Alopecia: Tumor Assessment Wk 012	-5.98 (± 25.39)			
Alopecia: Tumor Assessment Wk 018	-6.85 (± 24.59)			
Alopecia: Tumor Assessment Wk 024	-8.11 (± 24.16)			
Alopecia: Tumor Assessment Wk 030	-6.96 (± 25.93)			

Alopecia: Tumor Assessment Wk 036	-6.52 (± 25.79)			
Alopecia: Tumor Assessment Wk 042	-6.67 (± 26.13)			
Alopecia: Tumor Assessment Wk 048	-7.51 (± 26.55)			
Alopecia: Tumor Assessment Wk 054	2.56 (± 9.25)			
Alopecia: Tumor Assessment Wk 057	-6.43 (± 27.77)			
Alopecia: Tumor Assessment Wk 060	0.00 (± 15.71)			
Alopecia: Tumor Assessment Wk 066	-6.41 (± 26.44)			
Alopecia: Tumor Assessment Wk 072	9.52 (± 16.27)			
Alopecia: Tumor Assessment Wk 075	-6.67 (± 27.43)			
Alopecia: Tumor Assessment Wk 078	13.33 (± 18.26)			
Alopecia: Tumor Assessment Wk 084	-6.14 (± 26.68)			
Alopecia: Tumor Assessment Wk 090	5.56 (± 13.61)			
Alopecia: Tumor Assessment Wk 093	-4.76 (± 28.28)			
Alopecia: Tumor Assessment Wk 096	6.67 (± 14.91)			
Alopecia: Tumor Assessment Wk 102	-4.76 (± 26.78)			
Alopecia: Tumor Assessment Wk 108	20.00 (± 18.26)			
Alopecia: Tumor Assessment Wk 111	-3.17 (± 27.70)			
Alopecia: Tumor Assessment Wk 114	16.67 (± 23.57)			
Alopecia: Tumor Assessment Wk 120	3.51 (± 29.18)			
Alopecia: Tumor Assessment Wk 126	22.22 (± 19.25)			
Alopecia: Tumor Assessment Wk 129	5.88 (± 17.62)			
Alopecia: Tumor Assessment Wk 132	0.00 (± 9999999)			
Alopecia: Tumor Assessment Wk 138	-4.76 (± 28.81)			
Alopecia: Tumor Assessment Wk 144	0.00 (± 9999999)			
Alopecia: Tumor Assessment Wk 147	-7.41 (± 36.43)			
Alopecia: Tumor Assessment Wk 156	-4.17 (± 45.21)			
Alopecia: Tumor Assessment Wk 165	0.00 (± 0.00)			
Alopecia: Tumor Assessment Wk 174	0.00 (± 9999999)			
Alopecia: Tumor Assessment Wk 183	33.33 (± 9999999)			
Pain in chest: Baseline	14.20 (± 21.62)			
Pain in chest: C2D1	0.13 (± 19.74)			
Pain in chest: Tumor Assessment Wk 006	0.10 (± 23.99)			
Pain in chest: Tumor Assessment Wk 012	-0.75 (± 22.35)			
Pain in chest: Tumor Assessment Wk 018	-1.12 (± 18.38)			

Pain in chest: Tumor Assessment Wk 024	-2.74 (± 18.16)			
Pain in chest: Tumor Assessment Wk 030	-1.77 (± 20.82)			
Pain in chest: Tumor Assessment Wk 036	-2.96 (± 20.39)			
Pain in chest: Tumor Assessment Wk 042	-2.41 (± 20.02)			
Pain in chest: Tumor Assessment Wk 048	-4.35 (± 22.80)			
Pain in chest: Tumor Assessment Wk 054	0.00 (± 20.10)			
Pain in chest: Tumor Assessment Wk 057	-6.06 (± 21.36)			
Pain in chest: Tumor Assessment Wk 060	7.41 (± 22.22)			
Pain in chest: Tumor Assessment Wk 066	-3.33 (± 20.48)			
Pain in chest: Tumor Assessment Wk 072	-14.29 (± 17.82)			
Pain in chest: Tumor Assessment Wk 075	-6.14 (± 18.75)			
Pain in chest: Tumor Assessment Wk 078	-16.67 (± 19.25)			
Pain in chest: Tumor Assessment Wk 084	-7.41 (± 16.16)			
Pain in chest: Tumor Assessment Wk 090	-6.67 (± 14.91)			
Pain in chest: Tumor Assessment Wk 093	-1.33 (± 15.15)			
Pain in chest: Tumor Assessment Wk 096	-8.33 (± 16.67)			
Pain in chest: Tumor Assessment Wk 102	-8.97 (± 15.08)			
Pain in chest: Tumor Assessment Wk 108	-13.33 (± 18.26)			
Pain in chest: Tumor Assessment Wk 111	-5.00 (± 16.31)			
Pain in chest: Tumor Assessment Wk 114	-33.33 (± 0.00)			
Pain in chest: Tumor Assessment Wk 120	-7.41 (± 18.28)			
Pain in chest: Tumor Assessment Wk 126	-11.11 (± 19.25)			
Pain in chest: Tumor Assessment Wk 129	-6.25 (± 18.13)			
Pain in chest: Tumor Assessment Wk 132	-33.33 (± 9999999)			
Pain in chest: Tumor Assessment Wk 138	-5.13 (± 22.96)			
Pain in chest: Tumor Assessment Wk 144	-33.33 (± 9999999)			
Pain in chest: Tumor Assessment Wk 147	-4.17 (± 21.36)			
Pain in chest: Tumor Assessment Wk 156	-9.52 (± 16.27)			
Pain in chest: Tumor Assessment Wk 165	11.11 (± 19.25)			
Pain in chest: Tumor Assessment Wk 174	0.00 (± 9999999)			
Pain in chest: Tumor Assessment Wk 183	33.33 (± 9999999)			

Pain in arm or shoulder: Baseline	16.09 (± 24.63)			
Pain in arm or shoulder: C2D1	1.81 (± 21.67)			
Pain in arm or shoulder: Tumor Assessment Wk 006	-0.30 (± 23.85)			
Pain in arm or shoulder: Tumor Assessment Wk 012	0.75 (± 24.09)			
Pain in arm or shoulder: Tumor Assessment Wk 018	3.15 (± 28.78)			
Pain in arm or shoulder: Tumor Assessment Wk 024	-0.68 (± 23.56)			
Pain in arm or shoulder: Tumor Assessment Wk 030	0.00 (± 25.86)			
Pain in arm or shoulder: Tumor Assessment Wk 036	-2.20 (± 22.11)			
Pain in arm or shoulder: Tumor Assessment Wk 042	-1.19 (± 24.51)			
Pain in arm or shoulder: Tumor Assessment Wk 048	-2.38 (± 24.95)			
Pain in arm or shoulder: Tumor Assessment Wk 054	2.56 (± 21.35)			
Pain in arm or shoulder: Tumor Assessment Wk 057	1.72 (± 26.80)			
Pain in arm or shoulder: Tumor Assessment Wk 060	-6.67 (± 21.08)			
Pain in arm or shoulder: Tumor Assessment Wk 066	0.64 (± 21.38)			
Pain in arm or shoulder: Tumor Assessment Wk 072	4.76 (± 23.00)			
Pain in arm or shoulder: Tumor Assessment Wk 075	-4.27 (± 23.17)			
Pain in arm or shoulder: Tumor Assessment Wk 078	16.67 (± 19.25)			
Pain in arm or shoulder: Tumor Assessment Wk 084	-9.01 (± 23.11)			
Pain in arm or shoulder: Tumor Assessment Wk 090	0.00 (± 23.57)			
Pain in arm or shoulder: Tumor Assessment Wk 093	-9.88 (± 20.29)			
Pain in arm or shoulder: Tumor Assessment Wk 096	-8.33 (± 16.67)			
Pain in arm or shoulder: Tumor Assessment Wk 102	-4.94 (± 20.05)			
Pain in arm or shoulder: Tumor Assessment Wk 108	0.00 (± 23.57)			
Pain in arm or shoulder: Tumor Assessment Wk 111	-6.35 (± 20.05)			
Pain in arm or shoulder: Tumor Assessment Wk 114	16.67 (± 23.57)			
Pain in arm or shoulder: Tumor Assessment Wk 120	-7.02 (± 21.02)			
Pain in arm or shoulder: Tumor Assessment Wk 126	22.22 (± 19.25)			
Pain in arm or shoulder: Tumor Assessment Wk 129	-7.84 (± 18.74)			
Pain in arm or shoulder: Tumor Assessment Wk 132	0.00 (± 9999999)			
Pain in arm or shoulder: Tumor Assessment Wk 138	-11.90 (± 16.57)			
Pain in arm or shoulder: Tumor Assessment Wk 144	-33.33 (± 9999999)			

Pain in arm or shoulder: Tumor Assessment Wk 147	-11.11 (± 16.67)			
Pain in arm or shoulder: Tumor Assessment Wk 156	-12.50 (± 17.25)			
Pain in arm or shoulder: Tumor Assessment Wk 165	-11.11 (± 19.25)			
Pain in arm or shoulder: Tumor Assessment Wk 174	-33.33 (± 9999999)			
Pain in arm or shoulder: Tumor Assessment Wk 183	0.00 (± 9999999)			
Pain in other parts: Baseline	25.46 (± 30.26)			
Pain in other parts: C2D1	-0.49 (± 27.84)			
Pain in other parts: Tumor Assessment Wk 006	1.12 (± 31.80)			
Pain in other parts: Tumor Assessment Wk 012	0.93 (± 28.33)			
Pain in other parts: Tumor Assessment Wk 018	-1.19 (± 23.89)			
Pain in other parts: Tumor Assessment Wk 024	-1.41 (± 23.11)			
Pain in other parts: Tumor Assessment Wk 030	-0.62 (± 21.95)			
Pain in other parts: Tumor Assessment Wk 036	-4.17 (± 19.45)			
Pain in other parts: Tumor Assessment Wk 042	-4.17 (± 24.52)			
Pain in other parts: Tumor Assessment Wk 048	-0.98 (± 23.72)			
Pain in other parts: Tumor Assessment Wk 054	11.11 (± 16.41)			
Pain in other parts: Tumor Assessment Wk 057	-5.23 (± 20.41)			
Pain in other parts: Tumor Assessment Wk 060	3.70 (± 11.11)			
Pain in other parts: Tumor Assessment Wk 066	-0.67 (± 27.35)			
Pain in other parts: Tumor Assessment Wk 072	4.76 (± 12.60)			
Pain in other parts: Tumor Assessment Wk 075	-2.70 (± 25.31)			
Pain in other parts: Tumor Assessment Wk 078	16.67 (± 19.25)			
Pain in other parts: Tumor Assessment Wk 084	-3.92 (± 26.92)			
Pain in other parts: Tumor Assessment Wk 090	6.67 (± 14.91)			
Pain in other parts: Tumor Assessment Wk 093	-10.26 (± 22.65)			
Pain in other parts: Tumor Assessment Wk 096	0.00 (± 0.00)			
Pain in other parts: Tumor Assessment Wk 102	-8.97 (± 22.23)			
Pain in other parts: Tumor Assessment Wk 108	6.67 (± 14.91)			
Pain in other parts: Tumor Assessment Wk 111	-8.33 (± 28.36)			
Pain in other parts: Tumor Assessment Wk 114	16.67 (± 23.57)			
Pain in other parts: Tumor Assessment Wk 120	-3.92 (± 20.01)			

Pain in other parts: Tumor Assessment Wk 126	33.33 (± 33.33)			
Pain in other parts: Tumor Assessment Wk 129	-6.25 (± 18.13)			
Pain in other parts: Tumor Assessment Wk 132	0.00 (± 9999999)			
Pain in other parts: Tumor Assessment Wk 138	-10.26 (± 21.01)			
Pain in other parts: Tumor Assessment Wk 144	0.00 (± 9999999)			
Pain in other parts: Tumor Assessment Wk 147	-12.50 (± 24.80)			
Pain in other parts: Tumor Assessment Wk 156	-14.29 (± 17.82)			
Pain in other parts: Tumor Assessment Wk 165	0.00 (± 0.00)			
Pain in other parts: Tumor Assessment Wk 174	0.00 (± 9999999)			
Pain in other parts: Tumor Assessment Wk 183	0.00 (± 9999999)			
Dyspnoea at Resting: Baseline	10.47 (± 19.79)			
Dyspnoea at Resting: C2D1	2.53 (± 19.17)			
Dyspnoea at Resting: Tumor Assessment Wk 006	1.68 (± 20.59)			
Dyspnoea at Resting: Tumor Assessment Wk 012	1.65 (± 19.61)			
Dyspnoea at Resting: Tumor Assessment Wk 018	1.83 (± 17.07)			
Dyspnoea at Resting: Tumor Assessment Wk 024	-0.23 (± 15.90)			
Dyspnoea at Resting: Tumor Assessment Wk 030	2.03 (± 21.76)			
Dyspnoea at Resting: Tumor Assessment Wk 036	0.37 (± 20.18)			
Dyspnoea at Resting: Tumor Assessment Wk 042	-0.40 (± 19.01)			
Dyspnoea at Resting: Tumor Assessment Wk 048	0.95 (± 17.92)			
Dyspnoea at Resting: Tumor Assessment Wk 054	2.38 (± 8.91)			
Dyspnoea at Resting: Tumor Assessment Wk 057	-2.38 (± 19.96)			
Dyspnoea at Resting: Tumor Assessment Wk 060	0.00 (± 0.00)			
Dyspnoea at Resting: Tumor Assessment Wk 066	3.27 (± 17.96)			
Dyspnoea at Resting: Tumor Assessment Wk 072	9.52 (± 31.71)			
Dyspnoea at Resting: Tumor Assessment Wk 075	-0.83 (± 17.68)			
Dyspnoea at Resting: Tumor Assessment Wk 078	20.00 (± 50.55)			
Dyspnoea at Resting: Tumor Assessment Wk 084	-0.88 (± 16.42)			
Dyspnoea at Resting: Tumor Assessment Wk 090	11.11 (± 45.54)			
Dyspnoea at Resting: Tumor Assessment Wk 093	4.76 (± 23.51)			
Dyspnoea at Resting: Tumor Assessment Wk 096	13.33 (± 29.81)			

Dyspnoea at Resting: Tumor Assessment Wk 102	-1.19 (± 16.93)			
Dyspnoea at Resting: Tumor Assessment Wk 108	-6.67 (± 27.89)			
Dyspnoea at Resting: Tumor Assessment Wk 111	-1.59 (± 16.59)			
Dyspnoea at Resting: Tumor Assessment Wk 114	-16.67 (± 23.57)			
Dyspnoea at Resting: Tumor Assessment Wk 120	-1.75 (± 13.49)			
Dyspnoea at Resting: Tumor Assessment Wk 126	-11.11 (± 19.25)			
Dyspnoea at Resting: Tumor Assessment Wk 129	-1.96 (± 14.29)			
Dyspnoea at Resting: Tumor Assessment Wk 132	0.00 (± 9999999)			
Dyspnoea at Resting: Tumor Assessment Wk 138	7.69 (± 19.97)			
Dyspnoea at Resting: Tumor Assessment Wk 144	0.00 (± 9999999)			
Dyspnoea at Resting: Tumor Assessment Wk 147	7.41 (± 14.70)			
Dyspnoea at Resting: Tumor Assessment Wk 156	20.83 (± 17.25)			
Dyspnoea at Resting: Tumor Assessment Wk 165	11.11 (± 19.25)			
Dyspnoea at Resting: Tumor Assessment Wk 174	0.00 (± 9999999)			
Dyspnoea at Resting: Tumor Assessment Wk 183	33.33 (± 9999999)			
Dyspnoea at Walking: Baseline	27.31 (± 26.59)			
Dyspnoea at Walking: C2D1	2.52 (± 21.43)			
Dyspnoea at Walking: Tumor Assessment Wk 006	1.18 (± 23.65)			
Dyspnoea at Walking: Tumor Assessment Wk 012	-1.21 (± 26.37)			
Dyspnoea at Walking: Tumor Assessment Wk 018	-1.29 (± 24.94)			
Dyspnoea at Walking: Tumor Assessment Wk 024	-3.83 (± 26.23)			
Dyspnoea at Walking: Tumor Assessment Wk 030	-2.32 (± 26.39)			
Dyspnoea at Walking: Tumor Assessment Wk 036	-3.94 (± 27.74)			
Dyspnoea at Walking: Tumor Assessment Wk 042	-3.88 (± 25.78)			
Dyspnoea at Walking: Tumor Assessment Wk 048	-6.48 (± 27.77)			
Dyspnoea at Walking: Tumor Assessment Wk 054	2.38 (± 27.62)			
Dyspnoea at Walking: Tumor Assessment Wk 057	-7.02 (± 23.35)			
Dyspnoea at Walking: Tumor Assessment Wk 060	-3.03 (± 17.98)			
Dyspnoea at Walking: Tumor Assessment Wk 066	-1.89 (± 25.67)			
Dyspnoea at Walking: Tumor Assessment Wk 072	4.76 (± 29.99)			
Dyspnoea at Walking: Tumor Assessment Wk 075	-4.17 (± 22.88)			

Dyspnoea at Walking: Tumor Assessment Wk 078	-6.67 (± 54.77)			
Dyspnoea at Walking: Tumor Assessment Wk 084	-6.14 (± 23.06)			
Dyspnoea at Walking: Tumor Assessment Wk 090	-5.56 (± 38.97)			
Dyspnoea at Walking: Tumor Assessment Wk 093	-5.95 (± 24.09)			
Dyspnoea at Walking: Tumor Assessment Wk 096	13.33 (± 38.01)			
Dyspnoea at Walking: Tumor Assessment Wk 102	-8.33 (± 26.64)			
Dyspnoea at Walking: Tumor Assessment Wk 108	-20.00 (± 29.81)			
Dyspnoea at Walking: Tumor Assessment Wk 111	-9.52 (± 26.13)			
Dyspnoea at Walking: Tumor Assessment Wk 114	-16.67 (± 23.57)			
Dyspnoea at Walking: Tumor Assessment Wk 120	-7.02 (± 21.02)			
Dyspnoea at Walking: Tumor Assessment Wk 126	-33.33 (± 33.33)			
Dyspnoea at Walking: Tumor Assessment Wk 129	-9.80 (± 19.60)			
Dyspnoea at Walking: Tumor Assessment Wk 132	-33.33 (± 9999999)			
Dyspnoea at Walking: Tumor Assessment Wk 138	-2.38 (± 24.33)			
Dyspnoea at Walking: Tumor Assessment Wk 144	0.00 (± 9999999)			
Dyspnoea at Walking: Tumor Assessment Wk 147	-3.70 (± 26.06)			
Dyspnoea at Walking: Tumor Assessment Wk 156	4.17 (± 37.53)			
Dyspnoea at Walking: Tumor Assessment Wk 165	11.11 (± 38.49)			
Dyspnoea at Walking: Tumor Assessment Wk 174	0.00 (± 9999999)			
Dyspnoea at Walking: Tumor Assessment Wk 183	-33.33 (± 9999999)			
Dyspnoea at Climbing Stairs: Baseline	37.12 (± 29.57)			
Dyspnoea at Climbing Stairs: C2D1	2.23 (± 22.71)			
Dyspnoea at Climbing Stairs: Tumor Asses. Wk 006	1.39 (± 26.23)			
Dyspnoea at Climbing Stairs: Tumor Asses. Wk 012	-1.66 (± 27.20)			
Dyspnoea at Climbing Stairs: Tumor Asses. Wk 018	-2.04 (± 26.17)			
Dyspnoea at Climbing Stairs: Tumor Asses. Wk 024	-4.73 (± 24.90)			
Dyspnoea at Climbing Stairs: Tumor Asses. Wk 030	-2.61 (± 28.66)			
Dyspnoea at Climbing Stairs: Tumor Asses. Wk 036	-6.81 (± 29.72)			
Dyspnoea at Climbing Stairs: Tumor Asses. Wk 042	-5.81 (± 26.17)			
Dyspnoea at Climbing Stairs: Tumor Asses. Wk 048	-3.70 (± 29.37)			
Dyspnoea at Climbing Stairs: Tumor Asses. Wk 054	2.38 (± 24.33)			

Dyspnoea at Climbing Stairs: Tumor Asses. Wk 057	-6.90 (± 27.75)			
Dyspnoea at Climbing Stairs: Tumor Asses. Wk 060	-3.03 (± 17.98)			
Dyspnoea at Climbing Stairs: Tumor Asses. Wk 066	1.89 (± 26.49)			
Dyspnoea at Climbing Stairs: Tumor Asses. Wk 072	0.00 (± 33.33)			
Dyspnoea at Climbing Stairs: Tumor Asses. Wk 075	-1.67 (± 28.19)			
Dyspnoea at Climbing Stairs: Tumor Asses. Wk 078	-13.33 (± 29.81)			
Dyspnoea at Climbing Stairs: Tumor Asses. Wk 084	-1.75 (± 24.44)			
Dyspnoea at Climbing Stairs: Tumor Asses. Wk 090	-26.67 (± 14.91)			
Dyspnoea at Climbing Stairs: Tumor Asses. Wk 093	-9.52 (± 23.76)			
Dyspnoea at Climbing Stairs: Tumor Asses. Wk 096	13.33 (± 29.81)			
Dyspnoea at Climbing Stairs: Tumor Asses. Wk 102	-8.33 (± 26.64)			
Dyspnoea at Climbing Stairs: Tumor Asses. Wk 108	0.00 (± 33.33)			
Dyspnoea at Climbing Stairs: Tumor Asses. Wk 111	-9.52 (± 23.90)			
Dyspnoea at Climbing Stairs: Tumor Asses. Wk 114	-16.67 (± 23.57)			
Dyspnoea at Climbing Stairs: Tumor Asses. Wk 120	-8.77 (± 18.73)			
Dyspnoea at Climbing Stairs: Tumor Asses. Wk 126	-11.11 (± 38.49)			
Dyspnoea at Climbing Stairs: Tumor Asses. Wk 129	-9.80 (± 22.87)			
Dyspnoea at Climbing Stairs: Tumor Asses. Wk 132	-33.33 (± 9999999)			
Dyspnoea at Climbing Stairs: Tumor Asses. Wk 138	-11.90 (± 24.83)			
Dyspnoea at Climbing Stairs: Tumor Asses. Wk 144	0.00 (± 9999999)			
Dyspnoea at Climbing Stairs: Tumor Asses. Wk 147	-14.81 (± 17.57)			
Dyspnoea at Climbing Stairs: Tumor Asses. Wk 156	-4.17 (± 27.82)			
Dyspnoea at Climbing Stairs: Tumor Asses. Wk 165	-11.11 (± 19.25)			
Dyspnoea at Climbing Stairs: Tumor Asses. Wk 174	0.00 (± 9999999)			
Dyspnoea at Climbing Stairs: Tumor Asses. Wk 183	-33.33 (± 9999999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival Based on Disease Status as Evaluated By the Investigator in Accordance With Modified RECIST

End point title	Progression-Free Survival Based on Disease Status as

	Evaluated By the Investigator in Accordance With Modified RECIST

End point description:

PFS was defined as the time (in months) from initiation of study treatment to the first documented disease progression or death from any cause, whichever occurred first. PFS will be calculated based on disease status evaluated by the investigator according to modified RECIST. The safety population was based on all participants who received any dose of atezolizumab during the study treatment.This was a single-arm study. The study population was participants with Stage IIIB or Stage IV NSCLC. The primary objective of this study was to understand the safety in this participant population (without distinction of Stage IIIB and IV) and it was not planned to analyze them separately as per the protocol.

End point type	Secondary

End point timeframe:

Baseline up to disease progression or death whichever occurs first (up to 4 years)

End point values	Atezolizumab			
Subject group type	Reporting group			
Number of subjects analysed	615			
Units: Months				
median (confidence interval 95%)	3.7 (3.0 to 4.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Alive 3 Years After Initiation of Treatment

End point title	Percentage of Participants Alive 3 Years After Initiation of Treatment

End point description:

The OS rate at 3 years, was defined as the percentage of participants remaining alive 3 years after initiation of study treatment. The safety population was based on all participants who received any dose of atezolizumab during the study treatment.

End point type	Secondary

End point timeframe:

Baseline up to Year 3

End point values	Atezolizumab			
Subject group type	Reporting group			
Number of subjects analysed	615			
Units: Percentage of Participants				
number (not applicable)	19.6			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response as Assessed by the Investigator According to RECIST v.1.1

End point title	Duration of Response as Assessed by the Investigator According to RECIST v.1.1

End point description:

DOR was defined as the time from the first tumor assessment that supported the participant’s objective response (CR or PR, whichever was first reported) to documented disease progression as determined by the investigator according to RECIST v1.1 or death from any cause, whichever occurred first, among participants who had a best overall response as CR or PR. The safety population was based on all participants who received any dose of atezolizumab during the study treatment.

End point type	Secondary

End point timeframe:

From date of first objective response up to disease progression or death whichever occurs first (up to 4 years)

End point values	Atezolizumab			
Subject group type	Reporting group			
Number of subjects analysed	615			
Units: Months				
median (confidence interval 95%)	16.6 (9.7 to 20.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response as Assessed by the Investigator According to Modified RECIST

End point title	Duration of Response as Assessed by the Investigator According to Modified RECIST

End point description:

DOR was defined as the duration from the first tumor assessment that supports the participant's objective response (CR or PR, whichever is first recorded) to disease progression or death due to any cause, whichever occurred first. The safety population was based on all participants who received any dose of atezolizumab during the study treatment.

End point type	Secondary

End point timeframe:

From date of first objective response up to disease progression or death whichever occurs first (up to 4 years)

End point values	Atezolizumab			
Subject group type	Reporting group			
Number of subjects analysed	615			
Units: Months				
median (confidence interval 95%)	20.5 (16.6 to 28.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Objective Reponse as Assessed by the Investigator According to RECIST v1.1

End point title	Percentage of Participants with Objective Reponse as Assessed by the Investigator According to RECIST v1.1

End point description:

Objective response rate (ORR), according to RECIST v1.1, was defined as the percentage of participants with a confirmed best overall response (BOR), either complete response (CR) or partial response (PR), as determined by the investigator using RECIST v1.1. The safety population was based on all participants who received any dose of atezolizumab during the study treatment.

End point type	Secondary

End point timeframe:

Baseline up to disease progression or death whichever occurs first (up to 4 years)

End point values	Atezolizumab			
Subject group type	Reporting group			
Number of subjects analysed	615			
Units: Percentage of Participants				
number (not applicable)	11.5			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Objective Reponse as Assessed by the Investigator According to Modified RECIST

End point title	Percentage of Participants with Objective Reponse as Assessed by the Investigator According to Modified RECIST

End point description:

The investigator-assessed ORR was defined as the proportion of participants whose confirmed BOR is either a PR or CR per modified RECIST. The safety population was based on all participants who received any dose of atezolizumab during the study treatment.

End point type	Secondary

End point timeframe:

Baseline up to disease progression or death whichever occurs first (up to 4 years)

End point values	Atezolizumab			
Subject group type	Reporting group			
Number of subjects analysed	615			
Units: Percentage of Participants				
number (not applicable)	12.4			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to 4 years

Adverse event reporting additional description:

The ITT population consisted of 619 enrolled participants and the safety population consisted of the 615 participants who received at least one dose of atezolizumab, which was the primary analysis population for the study. Four enrolled participants died before receiving the treatment and were excluded from the safety population.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24

Reporting groups

Reporting group title	Atezolizumab

Reporting group description:

Participants with Stage IIIb or State IV NSCLC who had progressed after standard systemic chemotherapy received atezolizumab until Investigator-assessed loss of clinical benefit, unacceptable toxicity, investigator or participant's decision to withdraw from therapy, or death (whichever occurred first).

Serious adverse events	Atezolizumab		
Total subjects affected by serious adverse events			
subjects affected / exposed	198 / 615 (32.20%)		
number of deaths (all causes)	474		
number of deaths resulting from adverse events	8		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasm			
subjects affected / exposed	1 / 615 (0.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cancer pain			
subjects affected / exposed	1 / 615 (0.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tumour haemorrhage			
subjects affected / exposed	1 / 615 (0.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Bladder cancer				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Prostate cancer				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Tumour pain				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Peripheral ischaemia				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Hypertension				
subjects affected / exposed	2 / 615 (0.33%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Lymphoedema				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Embolism venous				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Peripheral artery thrombosis				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Jugular vein thrombosis				

subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Deep vein thrombosis				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Surgical and medical procedures				
Limb operation				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
General physical health deterioration				
subjects affected / exposed	2 / 615 (0.33%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	1 / 1			
Device related thrombosis				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sudden death				
subjects affected / exposed	2 / 615 (0.33%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 2			
Chest pain				
subjects affected / exposed	2 / 615 (0.33%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Fatigue				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Oedema peripheral				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Asthenia				
subjects affected / exposed	2 / 615 (0.33%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Systemic inflammatory response syndrome				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			
Malaise				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	7 / 615 (1.14%)			
occurrences causally related to treatment / all	4 / 8			
deaths causally related to treatment / all	0 / 0			
Death				
subjects affected / exposed	2 / 615 (0.33%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 2			
Non-cardiac chest pain				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Influenza like illness				
subjects affected / exposed	2 / 615 (0.33%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Immune system disorders				

Anaphylactic shock			
subjects affected / exposed	2 / 615 (0.33%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Anaphylactic reaction			
subjects affected / exposed	1 / 615 (0.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	1 / 615 (0.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 615 (0.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Pneumothorax			
subjects affected / exposed	2 / 615 (0.33%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Hydrothorax			
subjects affected / exposed	1 / 615 (0.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haemoptysis			
subjects affected / exposed	3 / 615 (0.49%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Pleural effusion			

subjects affected / exposed	4 / 615 (0.65%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Cough				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Asthma				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	6 / 615 (0.98%)			
occurrences causally related to treatment / all	1 / 6			
deaths causally related to treatment / all	0 / 2			
Dyspnoea				
subjects affected / exposed	9 / 615 (1.46%)			
occurrences causally related to treatment / all	0 / 9			
deaths causally related to treatment / all	0 / 0			
Bronchial haemorrhage				
subjects affected / exposed	3 / 615 (0.49%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 1			
Pneumonitis				
subjects affected / exposed	10 / 615 (1.63%)			
occurrences causally related to treatment / all	9 / 10			
deaths causally related to treatment / all	1 / 1			
Respiratory failure				
subjects affected / exposed	4 / 615 (0.65%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 2			
Pneumothorax spontaneous				

subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Acute respiratory failure				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia aspiration				
subjects affected / exposed	2 / 615 (0.33%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 2			
Respiratory distress				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Chronic obstructive pulmonary disease				
subjects affected / exposed	5 / 615 (0.81%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Obstructive airways disorder				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Delirium				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Investigations				
Weight decreased				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Gamma-glutamyltransferase increased				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatic enzyme increased				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Blood alkaline phosphatase increased				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Ankle fracture				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Joint dislocation				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bone contusion				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infusion related reaction				
subjects affected / exposed	5 / 615 (0.81%)			
occurrences causally related to treatment / all	5 / 5			
deaths causally related to treatment / all	0 / 0			
Spinal cord injury				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Spinal compression fracture				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Spinal fracture				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Femur fracture				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Pericarditis				
subjects affected / exposed	4 / 615 (0.65%)			
occurrences causally related to treatment / all	3 / 4			
deaths causally related to treatment / all	2 / 2			
Bradycardia				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Atrial fibrillation				
subjects affected / exposed	3 / 615 (0.49%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Cardiac arrest				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Cardiac failure				
subjects affected / exposed	2 / 615 (0.33%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Endocarditis noninfective				

subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Stress cardiomyopathy				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			
Acute coronary syndrome				
subjects affected / exposed	4 / 615 (0.65%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 1			
Acute myocardial infarction				
subjects affected / exposed	2 / 615 (0.33%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Atrial flutter				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Hemiparesis				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cerebral infarction				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Headache				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Syncope				

subjects affected / exposed	2 / 615 (0.33%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Epilepsy				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Neurological symptom				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Seizure				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Autonomic nervous system imbalance				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Status epilepticus				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Depressed level of consciousness				
subjects affected / exposed	2 / 615 (0.33%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Ischaemic stroke				
subjects affected / exposed	2 / 615 (0.33%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Immune thrombocytopenia				

subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Autoimmune haemolytic anaemia				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Duodenal ulcer perforation				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Stomatitis				
subjects affected / exposed	2 / 615 (0.33%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 1			
Vomiting				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Ileus				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pancreatitis				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Abdominal pain				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Oesophageal obstruction				

subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	2 / 615 (0.33%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Colitis				
subjects affected / exposed	4 / 615 (0.65%)			
occurrences causally related to treatment / all	3 / 4			
deaths causally related to treatment / all	0 / 0			
Constipation				
subjects affected / exposed	2 / 615 (0.33%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Pancreatitis acute				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Hepatic lesion				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Cholelithiasis				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatotoxicity				

subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Cholecystitis				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Stevens-Johnson syndrome				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Acute kidney injury				
subjects affected / exposed	3 / 615 (0.49%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Nephropathy toxic				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Renal failure				
subjects affected / exposed	2 / 615 (0.33%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Haematuria				
subjects affected / exposed	2 / 615 (0.33%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Hydronephrosis				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Endocrine disorders				

Adrenal insufficiency				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hyperthyroidism				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Primary adrenal insufficiency				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hypothyroidism				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Spinal pain				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Back pain				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Arthralgia				
subjects affected / exposed	3 / 615 (0.49%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal chest pain				
subjects affected / exposed	2 / 615 (0.33%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			

Neck pain				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Erysipelas				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	35 / 615 (5.69%)			
occurrences causally related to treatment / all	2 / 39			
deaths causally related to treatment / all	1 / 5			
Upper respiratory tract infection				
subjects affected / exposed	4 / 615 (0.65%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Enterocolitis infectious				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
COVID-19				
subjects affected / exposed	2 / 615 (0.33%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Infective exacerbation of chronic obstructive airways disease				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Respiratory tract infection				
subjects affected / exposed	3 / 615 (0.49%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Pneumonia klebsiella				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lower respiratory tract infection				
subjects affected / exposed	11 / 615 (1.79%)			
occurrences causally related to treatment / all	0 / 12			
deaths causally related to treatment / all	0 / 1			
Encephalitis				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Herpes zoster				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Septic shock				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infected fistula				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Pleural infection				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diverticulitis				

subjects affected / exposed	2 / 615 (0.33%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Influenza				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Atypical pneumonia				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia streptococcal				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia escherichia				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	2 / 615 (0.33%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	1 / 1			
Liver abscess				
subjects affected / exposed	1 / 615 (0.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia bacterial				
subjects affected / exposed	2 / 615 (0.33%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Pulmonary sepsis				

subjects affected / exposed	1 / 615 (0.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Bacterial infection			
subjects affected / exposed	1 / 615 (0.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	1 / 615 (0.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypokalaemia			
subjects affected / exposed	1 / 615 (0.16%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Decreased appetite			
subjects affected / exposed	1 / 615 (0.16%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Type 2 diabetes mellitus			
subjects affected / exposed	1 / 615 (0.16%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Dehydration			
subjects affected / exposed	2 / 615 (0.33%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Atezolizumab		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	480 / 615 (78.05%)		
Nervous system disorders			
Headache			
subjects affected / exposed	44 / 615 (7.15%)		
occurrences (all)	47		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	93 / 615 (15.12%)		
occurrences (all)	123		
Pyrexia			
subjects affected / exposed	73 / 615 (11.87%)		
occurrences (all)	123		
Fatigue			
subjects affected / exposed	100 / 615 (16.26%)		
occurrences (all)	111		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	78 / 615 (12.68%)		
occurrences (all)	99		
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	46 / 615 (7.48%)		
occurrences (all)	59		
Diarrhoea			
subjects affected / exposed	72 / 615 (11.71%)		
occurrences (all)	97		
Nausea			
subjects affected / exposed	67 / 615 (10.89%)		
occurrences (all)	89		
Constipation			
subjects affected / exposed	55 / 615 (8.94%)		
occurrences (all)	68		
Respiratory, thoracic and mediastinal disorders			

Dyspnoea			
subjects affected / exposed	85 / 615 (13.82%)		
occurrences (all)	97		
Cough			
subjects affected / exposed	107 / 615 (17.40%)		
occurrences (all)	134		
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	46 / 615 (7.48%)		
occurrences (all)	55		
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	62 / 615 (10.08%)		
occurrences (all)	87		
Hyperthyroidism			
subjects affected / exposed	42 / 615 (6.83%)		
occurrences (all)	50		
Musculoskeletal and connective tissue disorders			
Musculoskeletal chest pain			
subjects affected / exposed	37 / 615 (6.02%)		
occurrences (all)	39		
Back pain			
subjects affected / exposed	63 / 615 (10.24%)		
occurrences (all)	76		
Pain in extremity			
subjects affected / exposed	39 / 615 (6.34%)		
occurrences (all)	45		
Arthralgia			
subjects affected / exposed	83 / 615 (13.50%)		
occurrences (all)	102		
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	43 / 615 (6.99%)		
occurrences (all)	60		
Upper respiratory tract infection			

subjects affected / exposed	36 / 615 (5.85%)		
occurrences (all)	44		
Nasopharyngitis			
subjects affected / exposed	35 / 615 (5.69%)		
occurrences (all)	44		
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	33 / 615 (5.37%)		
occurrences (all)	40		
Decreased appetite			
subjects affected / exposed	104 / 615 (16.91%)		
occurrences (all)	116		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 January 2018	The following updates were made: [1] Background information on atezolizumab was updated; [2] Epidermal growth factor receptor/echinoderm microtubule-associated protein-like 4−anaplastic lymphoma kinase (EGFR/ALK) testing was only mandatory for participants with non-squamous non-small cell lung cancer (NSCLC); [3] The number and sequence of allowed tyrosine kinase inhibitor (TKIs) in eligible participants has been addressed; [4] Appendix 8 was added; [5] Participants with previously detected EGFRT70M mutation who experienced disease progression were with osimertinib were eligible; [6] Participants who were HIV-positive were allowed in the trial; [7] Further detail was provided related to the medical history and demographic data collected in this study during the Screening Period; [8] Sections 4.5.7. and 5.1.2 were updated; [9] Language describing immune-related myocarditis associated with atezolizumab was removed from the protocol; [10] Exploratory efficacy endpoints were revised; [11] An optional substudy was added to the trial; [12] Language was changed throughout the protocol to 'prior to study treatment initiation.'
14 January 2019	The following updates were made: [1] An appendix was added regarding the risks associated with atezolizumab and guidelines for management of adverse events (AEs) associated with atezolizumab; [2] Updated the dissemination of data and protection of trade secrets, including additional information on confidentiality of study data to reflect GDPR requirements.
17 December 2019	The following updates were made: [1] Text was modified to define special situations and detail how to record and report them; [2] Traditional herbal medicines could be used at the investigator’s discretion; [3] Clarification on timing of destruction of biological samples; [4] Language was added to clarify that research biosample repository (RBR) samples would destroyed; [5] Instructions about participant withdrawal from the RBR after site closure was modified; [6] The list of atezolizumab risks was updated; [7] Myositis was included in the guidelines for managing participants with atezolizumab associated AEs; [8] the description and management guidelines of systemic immune activation were replaced with descriptions and guidelines for hemophagocytic lymphohistiocytosis and macrophage activation syndrome; [9] The adverse event of special interest (AESI) of hypophysitis was added; [10] Reporting term 'sudden' death' was updated; [11] Text was modified to differentiate between spontaneous and therapeutic/elective abortions and how they were reported; [12] the atezolizumab AE management guidelines were revised to add laboratory and cardiac imaging abnormalities as signs or symptoms that are suggestive of myocarditis; [13] Additional clarifications were included.

23 March 2021	The following updates were made: [1] Approved indications for atezolizumab were added; [2] Text describing the current knowledge and risks of COVID-19 infection were highlighted; [3] Language was added to indicate that sites should confirm that appropriate temperature conditions were maintained during IMP transit and that the sites were responsible for maintaining records of IMP accountability during the study; [4] Immunosuppressive medications were removed from the prohibited therapy section and added to the permitted therapy section; [5] List of identified risks for atezolizumab was revised; [6] Text was added to clarify macrophage activation syndrome (MAS) as potential risks for atezolizumab; [7] HLH and MAS replaced systemic inflammatory response syndrome on the list of atezolizumab-associated AESIs; [8] Influenza-like illness was removed from the list of immediately reportable AESIs; [9] Text was added to clarify that AEs associated with special situations that also qualified as AESIs would be reported within 24 hours; [10] Text was added to indicate that the Informed Consent Form instruct female participants to inform the investigator if they became pregnant; [11] Updates to Appendix 5 to caution participants considering atezolizumab who had previously experienced a severe or life-threatening skin adverse reaction; [12] The management guidelines for infusion-related reactions associated with atezolizumab were updated; [13] Guidelines for management of atezolizumab-associated dermatological AEs were revised; [14] The management guidelines for Grade 4 myositis were removed; [15] The management guidelines for HLH and MAS were modified; [16] Additional clarifications were included.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported