Clinical trial results:
A Study of Atezolizumab Compared With a Single-Agent Chemotherapy in Treatment Naive Participants With Locally Advanced or Recurrent or Metastatic Non-Small Cell Lung Cancer Who Are Deemed Unsuitable For Platinum-Doublet Chemotherapy (IPSOS)

Summary

EudraCT number	2015-004105-16
Trial protocol	DE DK CZ GB PT PL ES IE BE SK BG IT RO
Global end of trial date	25 October 2023

Results information

Result version number	v2 (current)
This version publication date	16 October 2024
First version publication date	05 May 2023
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	MO29872

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03191786
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	F. Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4058
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	25 October 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	25 October 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study evaluated the efficacy and safety of atezolizumab compared with single agent chemotherapy with respect to antitumor effects in participants with treatment-naïve locally advanced or metastatic non-small cell lung cancer (NSCLC) who are deemed unsuitable for any platinum-doublet chemotherapy.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 September 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 7
Country: Number of subjects enrolled	Belgium: 8
Country: Number of subjects enrolled	Bulgaria: 6
Country: Number of subjects enrolled	Brazil: 20
Country: Number of subjects enrolled	Canada: 19
Country: Number of subjects enrolled	Switzerland: 11
Country: Number of subjects enrolled	China: 55
Country: Number of subjects enrolled	Colombia: 18
Country: Number of subjects enrolled	Czechia: 4
Country: Number of subjects enrolled	Germany: 42
Country: Number of subjects enrolled	Denmark: 3
Country: Number of subjects enrolled	Spain: 48
Country: Number of subjects enrolled	United Kingdom: 47
Country: Number of subjects enrolled	India: 38
Country: Number of subjects enrolled	Ireland: 4
Country: Number of subjects enrolled	Italy: 30
Country: Number of subjects enrolled	Kazakhstan: 8
Country: Number of subjects enrolled	Mexico: 16
Country: Number of subjects enrolled	Poland: 40
Country: Number of subjects enrolled	Portugal: 4
Country: Number of subjects enrolled	Romania: 6

Country: Number of subjects enrolled	Slovakia: 3
Country: Number of subjects enrolled	Viet Nam: 15
Country: Number of subjects enrolled	Luxembourg: 1
Worldwide total number of subjects	453
EEA total number of subjects	199

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)	65
From 65 to 84 years	364
85 years and over	24

Subject disposition

Recruitment

Recruitment details:

Participants diagnosed with advanced or recurrent (stage IIIb) or metastatic (stage IV) NSCLC took part in the study across 85 investigative sites in 23 countries from 11 Sep 2017 to 25 Oct 2023.

Pre-assignment

Screening details:

A total of 453 participants were randomized in 2:1 ratio to atezolizumab arm and single agent chemotherapy arm in this study. Of these 453, 447 participants received at least 1 dose of study treatment.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Atezolizumab

Arm description:

Participants received atezolizumab 1200 milligrams (mg), as intravenous (IV) infusion on Day 1 of each 21-day cycle until loss of clinical benefit, unacceptable toxicity, participant or physician decision to discontinue, or death.

Arm type	Experimental
Investigational medicinal product name	Atezolizumab
Investigational medicinal product code	
Other name	Tecentriq, MPDL3280A
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Atezolizumab was administered at a dose of 1200 mg, IV infusion on Day 1 of each 21-day cycle until loss of clinical benefit, unacceptable toxicity, participant or physician decision to discontinue, or death.

Arm title	Single Agent Chemotherapy (Vinorelbine or Gemcitabine)

Arm description:

Participants received single agent chemotherapy; either vinorelbine oral or IV, or gemcitabine IV, according to the label based on investigator’s choice until disease progression unacceptable toxicity, participant or physician decision to discontinue, or death.

Arm type	Active comparator
Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	
Other name	Gemzar
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Gemcitabine was administered per relevant local guidelines and SmPC management.

Investigational medicinal product name	Vinorelbine
Investigational medicinal product code	
Other name	Navelbine
Pharmaceutical forms	Capsule, Infusion
Routes of administration	Oral use, Intravenous use

Dosage and administration details:

Vinorelbine was administered per relevant local guidelines and Summary of Product Characteristics (SmPC) management.

Number of subjects in period 1	Atezolizumab	Single Agent Chemotherapy (Vinorelbine or Gemcitabine)
Started	302	151
Safety evaluable population	300	147
Completed	0	0
Not completed	302	151
Adverse event, serious fatal	236	127
Physician decision	1	-
Consent withdrawn by subject	26	16
Lost to follow-up	9	3
Moved to Post Trial Access Program	30	5

Baseline characteristics

Reporting groups	
Reporting group title	Atezolizumab
Reporting group description:	
Participants received atezolizumab 1200 milligrams (mg), as intravenous (IV) infusion on Day 1 of each 21-day cycle until loss of clinical benefit, unacceptable toxicity, participant or physician decision to discontinue, or death.	
Reporting group title	Single Agent Chemotherapy (Vinorelbine or Gemcitabine)
Reporting group description:	
Participants received single agent chemotherapy; either vinorelbine oral or IV, or gemcitabine IV, according to the label based on investigator's choice until disease progression unacceptable toxicity, participant or physician decision to discontinue, or death.	

Reporting group values	Atezolizumab	Single Agent Chemotherapy (Vinorelbine or Gemcitabine)	Total
Number of subjects	302	151	453
Age categorical Units: participants			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	46	19	65
From 65-84 years	241	123	364
85 years and over	15	9	24
Age Continuous Units: Years			
arithmetic mean	73.6	73.8	
standard deviation	± 9.1	± 8.5	-
Sex: Female, Male Units: Participants			
Female	82	43	125
Male	220	108	328
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	12	9	21
Asian	75	38	113
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	2	1	3
White	203	95	298
More than one race	6	6	12
Unknown or Not Reported	4	2	6
Ethnicity (NIH/OMB) Units: Subjects			

Hispanic or Latino	47	22	69
Not Hispanic or Latino	242	126	368
Unknown or Not Reported	13	3	16

End points

End points reporting groups

Reporting group title	Atezolizumab
Reporting group description:	
Participants received atezolizumab 1200 milligrams (mg), as intravenous (IV) infusion on Day 1 of each 21-day cycle until loss of clinical benefit, unacceptable toxicity, participant or physician decision to discontinue, or death.	
Reporting group title	Single Agent Chemotherapy (Vinorelbine or Gemcitabine)
Reporting group description:	
Participants received single agent chemotherapy; either vinorelbine oral or IV, or gemcitabine IV, according to the label based on investigator's choice until disease progression unacceptable toxicity, participant or physician decision to discontinue, or death.	

Primary: Overall Survival (OS)

End point title	Overall Survival (OS)
End point description:	
OS was defined as the time between the date of randomization and the date of death due to any cause. Kaplan-Meier (KM) estimates were used to calculate median. Intent-to-Treat (ITT) population included all randomized participants irrespective of whether the assigned treatment was actually received.	
End point type	Primary
End point timeframe:	
From randomization up to death from any cause (up to approximately 55 months)	

End point values	Atezolizumab	Single Agent Chemotherapy (Vinorelbine or Gemcitabine)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	302	151		
Units: Months				
median (confidence interval 95%)	10.3 (9.4 to 11.9)	9.2 (5.9 to 11.2)		

Statistical analyses

Statistical analysis title	OS Statistical Analysis
Statistical analysis description:	
Stratified analysis. Histologic subtype, PD-L1 IHC status and brain metastases (Yes/No) were added as stratification factors.	
Comparison groups	Atezolizumab v Single Agent Chemotherapy (Vinorelbine or Gemcitabine)

Number of subjects included in analysis	453
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.025
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.63
upper limit	0.97

Secondary: OS Rates at the 6, 12, 18, 24-Months Timepoints

End point title	OS Rates at the 6, 12, 18, 24-Months Timepoints

End point description:

OS was defined as the time between the date of randomization and the date of death due to any cause. OS rate at 6, 12, 18 and 24 months were estimated for each treatment arm using KM methodology. Percentages were rounded off to the nearest decimal point. ITT population included all randomized participants irrespective of whether the assigned treatment was actually received.

End point type	Secondary

End point timeframe:

6, 12, 18 and 24 months

End point values	Atezolizumab	Single Agent Chemotherapy (Vinorelbine or Gemcitabine)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	302	151		
Units: Percentage of participants				
number (confidence interval 95%)				
6 Months	64.0 (58.6 to 69.5)	57.5 (49.4 to 65.7)		
12 Months	43.7 (37.9 to 49.4)	38.6 (30.5 to 46.7)		
18 Months	31.4 (26.0 to 36.8)	24.0 (16.8 to 31.2)		
24 Months	24.3 (19.3 to 29.4)	12.4 (6.7 to 18.0)		

Statistical analyses

Statistical analysis title	OS Rate at 6 Months Statistical Analysis

Statistical analysis description:

OS Rate at 6 Months

Comparison groups	Atezolizumab v Single Agent Chemotherapy (Vinorelbine or

	Gemcitabine)
Number of subjects included in analysis	453
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in OS Rates
Point estimate	6.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.3
upper limit	16.3

Statistical analysis title	OS Rate at 24 Months Statistical Analysis
Statistical analysis description: OS Rate at 24 Months	
Comparison groups	Atezolizumab v Single Agent Chemotherapy (Vinorelbine or Gemcitabine)
Number of subjects included in analysis	453
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in OS Rates
Point estimate	11.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.4
upper limit	19.5

Statistical analysis title	OS Rate at 18 Months Statistical Analysis
Statistical analysis description: OS Rate at 18 Months	
Comparison groups	Atezolizumab v Single Agent Chemotherapy (Vinorelbine or Gemcitabine)
Number of subjects included in analysis	453
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in OS Rates
Point estimate	7.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	16.5

Statistical analysis title	OS Rate at 12 Months Statistical Analysis
Statistical analysis description: OS Rate at 12 Months	
Comparison groups	Atezolizumab v Single Agent Chemotherapy (Vinorelbine or Gemcitabine)
Number of subjects included in analysis	453
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in OS Rates
Point estimate	5.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.9
upper limit	15

Secondary: Percentage of Participants With Objective Response, as Determined by the Investigator Using Response Evaluation Criteria In Solid Tumors Version 1.1 (RECIST v1.1)

End point title	Percentage of Participants With Objective Response, as Determined by the Investigator Using Response Evaluation Criteria In Solid Tumors Version 1.1 (RECIST v1.1)

End point description:

Objective response rate (ORR)=best overall response(BOR) of either complete response(CR)/partial response(PR), as determined by investigator with use of RECIST v1.1. CR=disappearance of all target lesions/any pathological lymph nodes (target/non-target) having a reduction in short axis to <10 millimeters (mm). PR=at least 30% decrease in sum of diameters(SOD) of target lesions, taking as reference the baseline SOD. A minimum interval of 6 weeks (42 days) was considered for stable disease (SD) to be assigned as BOR, i.e. in case the single response is SD, PR/CR, this single response must be assessed no less than 6 weeks (42 days) after start date of study treatment. SD=neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference the smallest SOD while in the study. Percentages were rounded off to the nearest decimal point. ITT population=randomized participants irrespective of whether the assigned treatment was actually received.

End point type	Secondary

End point timeframe:

From randomization to the first occurence of disease progression or death from any cause, whichever occurs first (up to approximately 55 months)

End point values	Atezolizumab	Single Agent Chemotherapy (Vinorelbine or Gemcitabine)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	302	151		
Units: Percentage of participants				
number (confidence interval 95%)	16.9 (12.8 to 21.6)	7.9 (4.2 to 13.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival (PFS), as Determined by the Investigator Using RECIST v1.1

End point title	Progression-Free Survival (PFS), as Determined by the Investigator Using RECIST v1.1

End point description:

PFS was defined as the time from randomization to the first documented disease progression as determined by the investigator with the use of RECIST v1.1 or death from any cause, whichever occurs first. Progressive disease (PD) was defined as at least 20% increase in the sum of diameters of lesions, taking as reference the smallest sum during the study (nadir), including baseline. KM estimates were used to calculate median. ITT population included all randomized participants irrespective of whether the assigned treatment was actually received.

End point type	Secondary

End point timeframe:

From randomization to the first occurence of disease progression or death from any cause, whichever occurs first (up to approximately 55 months)

End point values	Atezolizumab	Single Agent Chemotherapy (Vinorelbine or Gemcitabine)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	302	151		
Units: Months				
median (confidence interval 95%)	4.2 (3.7 to 5.5)	4.0 (2.9 to 5.4)		

Statistical analyses

Statistical analysis title	PFS Statistical Analysis

Statistical analysis description:

Stratified analysis. Histologic subtype, PD-L1 IHC status and brain metastases (Yes/No) were added as stratification factors.

Comparison groups	Atezolizumab v Single Agent Chemotherapy (Vinorelbine or Gemcitabine)
Number of subjects included in analysis	453
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.182
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	1.07

Secondary: Percentage of Participants With At Least One Adverse Events (AE)

End point title	Percentage of Participants With At Least One Adverse Events (AE)

End point description:

An AE was any untoward medical occurrence in participant administered a pharmaceutical product & regardless of causal relationship with this treatment. An AE can therefore be any unfavorable & unintended sign (including an abnormal laboratory finding), symptom/disease temporally associated with use of investigational product, whether or not considered related to investigational product. AEs were reported based on the National Cancer Institute Common Terminology Criteria for AEs, version 4.0 (NCI-CTCAE, v4.0). Safety-evaluable population included all randomized participants who received any amount of study treatment.

End point type	Secondary

End point timeframe:

Baseline up to 90 days after last dose of atezolizumab (approximately 62 months)

End point values	Atezolizumab	Single Agent Chemotherapy (Vinorelbine or Gemcitabine)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	300	147		
Units: Percentage of participants				
number (not applicable)	91.7	97.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR), as Determined by the Investigator Using RECIST v1.1

End point title	Duration of Response (DOR), as Determined by the Investigator Using RECIST v1.1

End point description:

DOR= time from the first tumor assessment that supports the participants' objective response (CR or PR, whichever is first reported) to documented disease progression as determined by the investigator according to RECIST v1.1 or death from any cause, whichever occurs first, among participants who have a best overall response as CR or PR. CR=disappearance of all target lesions or any pathological lymph nodes (whether target or non-target) having a reduction in short axis to <10 mm. PR=at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum of diameters. PD=at least 20% increase in the sum of diameters of lesions, taking as reference the smallest sum during the study (nadir), including baseline. KM estimates were used to calculate median. ITT population=all randomized participants irrespective of whether the assigned treatment was actually received. Number analyzed is the number of participants with objective response (i.e. responders).

End point type	Secondary

End point timeframe:

Time from the first occurrence of a documented objective response to the time of disease progression or death from any cause, whichever occurs first (up to approximately 55 months)

End point values	Atezolizumab	Single Agent Chemotherapy (Vinorelbine or Gemcitabine)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	51	12		
Units: Months				
median (confidence interval 95%)	14.0 (8.1 to 20.3)	7.8 (4.8 to 9.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire – Core 30 (EORTC-QLQ-C30) Score

End point title	Change From Baseline in European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire – Core 30 (EORTC-QLQ-C30) Score

End point description:

EORTC QLQ-C30=30 questions that assess 5 aspects of patient functioning, 3 symptom scales, global health/quality of life, and 6 single items. All EORTC scales & single-item measures are linearly transformed so that each score has range of 0-100. A high score for functional/global health status scale represents high/healthy level of functioning/HRQoL (Health-Related Quality of Life); however high score for symptom scale/ item represents high level of symptomatology/problems. A ≥10-point change in symptoms subscale score was perceived as clinically significant. A positive change from baseline=improvement & negative change from baseline indicated worsening.'99999'=standard deviation (SD) non-estimable due to 1 participant evaluated.'00000'=data not reported due to no participant evaluated. ITT population=all randomized participants irrespective of whether the assigned treatment was actually received."n"=number of participants with data available for analysis at the specified timepoint.

End point type	Secondary

End point timeframe:

Baseline, Day 1 of each treatment cycle up to 30 days after last dose (up to approximately 55 months) (Cycle length = 21 days)

End point values	Atezolizumab	Single Agent Chemotherapy (Vinorelbine or Gemcitabine)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	302	151		
Units: units of a scale				
arithmetic mean (standard deviation)				
GHS/HRQoL Scale Score, Baseline (n=291, 146)	54.70 (± 22.00)	55.25 (± 21.06)		
GHS/HRQoL Scale Score, Week 6 (n=219, 115)	2.09 (± 24.11)	0.29 (± 22.94)		

GHS/HRQoL Scale Score, Week 12 (n=148, 63)	2.76 (± 23.42)	1.85 (± 19.94)		
GHS/HRQoL Scale Score, Week 18 (n=121, 40)	4.20 (± 24.27)	-0.42 (± 19.52)		
GHS/HRQoL Scale Score, Week 24 (n=105, 29)	4.92 (± 23.90)	-1.72 (± 18.82)		
GHS/HRQoL Scale Score, Week 30 (n=83, 22)	4.32 (± 21.12)	2.65 (± 13.70)		
GHS/HRQoL Scale Score, Week 36 (n=62, 16)	8.20 (± 23.55)	-0.52 (± 22.25)		
GHS/HRQoL Scale Score, Week 42 (n=54, 14)	6.17 (± 24.98)	1.19 (± 19.02)		
GHS/HRQoL Scale Score, Week 48 (n=44, 12)	6.44 (± 27.37)	4.86 (± 15.67)		
GHS/HRQoL Scale Score, Week 57 (n=37, 8)	8.56 (± 20.46)	8.33 (± 12.60)		
GHS/HRQoL Scale Score, Week 66 (n=33, 5)	6.82 (± 19.15)	5.00 (± 17.28)		
GHS/HRQoL Scale Score, Week 75 (n=26, 4)	3.85 (± 21.11)	2.08 (± 24.88)		
GHS/HRQoL Scale Score, Week 84 (n=19, 3)	11.40 (± 20.07)	-2.78 (± 12.73)		
GHS/HRQoL Scale Score, Week 93 (n=20, 2)	2.08 (± 24.61)	-12.50 (± 5.89)		
GHS/HRQoL Scale Score, Week 102 (n=16, 1)	4.69 (± 18.50)	-25.00 (± 99999)		
GHS/HRQoL Scale Score, Week 111 (n=14, 0)	1.79 (± 21.73)	00000 (± 00000)		
GHS/HRQoL Scale Score, Week 120 (n=14, 0)	2.38 (± 20.52)	00000 (± 00000)		
GHS/HRQoL Scale Score, Week 129 (n=14, 0)	-2.98 (± 19.78)	00000 (± 00000)		
GHS/HRQoL Scale Score, Week 138 (n=14, 0)	1.19 (± 25.91)	00000 (± 00000)		
GHS/HRQoL Scale Score, Week 147 (n=14, 0)	4.17 (± 18.42)	00000 (± 00000)		
GHS/HRQoL Scale Score, Week 156 (n=7, 0)	-2.38 (± 17.82)	00000 (± 00000)		
GHS/HRQoL Scale Score, Week 165 (n=8, 0)	-3.13 (± 23.54)	00000 (± 00000)		
GHS/HRQoL Scale Score, Week 174 (n=7, 0)	-2.38 (± 17.82)	00000 (± 00000)		
GHS/HRQoL Scale Score, Week 183 (n=5, 0)	-6.67 (± 19.00)	00000 (± 00000)		
GHS/HRQoL Scale Score, Week 192 (n=4, 0)	-4.17 (± 20.97)	00000 (± 00000)		
GHS/HRQoL Scale Score, Week 201 (n=2, 0)	0.00 (± 0.00)	00000 (± 00000)		
GHS/HRQoL Scale Score, Week 210 (n=1, 0)	-16.67 (± 99999)	00000 (± 00000)		
GHS/HRQoL Scale Score, SFUV (n=11, 13)	-9.85 (± 24.10)	3.85 (± 20.30)		
Physical Functioning, Baseline (n=294, 146)	61.34 (± 25.66)	61.97 (± 23.75)		
Physical Functioning, Week 6 (n=221, 115)	-2.93 (± 17.69)	-1.07 (± 18.49)		
Physical Functioning, Week 12 (n=149, 64)	0.17 (± 20.35)	1.46 (± 18.07)		
Physical Functioning, Week 18 (n=121, 39)	3.02 (± 17.97)	-1.58 (± 18.00)		
Physical Functioning, Week 24 (n=107, 30)	3.49 (± 18.66)	-5.50 (± 15.64)		

Physical Functioning, Week 30 (n=84, 23)	4.25 (± 18.22)	-1.23 (± 21.80)		
Physical Functioning, Week 36 (n=63, 16)	6.98 (± 19.68)	-4.90 (± 28.33)		
Physical Functioning, Week 42 (n=54, 14)	3.58 (± 24.08)	0.95 (± 16.92)		
Physical Functioning, Week 48 (n=43, 12)	7.44 (± 18.92)	2.22 (± 19.76)		
Physical Functioning, Week 57 (n=36, 8)	7.59 (± 16.73)	-3.33 (± 20.47)		
Physical Functioning, Week 66 (n=33, 5)	4.65 (± 22.39)	2.67 (± 17.38)		
Physical Functioning, Week 75 (n=26, 4)	4.87 (± 27.88)	-1.67 (± 34.16)		
Physical Functioning, Week 84 (n=18, 3)	3.70 (± 23.68)	-8.89 (± 26.94)		
Physical Functioning, Week 93 (n=20, 2)	1.67 (± 23.38)	-26.67 (± 18.86)		
Physical Functioning, Week 102 (n=16, 1)	2.40 (± 16.19)	-40.00 (± 99999)		
Physical Functioning, Week 111 (n=14, 0)	2.38 (± 19.67)	00000 (± 00000)		
Physical Functioning, Week 120 (n=14, 0)	3.33 (± 20.04)	00000 (± 00000)		
Physical Functioning, Week 129 (n=13, 0)	-1.03 (± 19.02)	00000 (± 00000)		
Physical Functioning, Week 138 (n=14, 0)	-0.48 (± 19.47)	00000 (± 00000)		
Physical Functioning, Week 147 (n=14, 0)	-0.48 (± 17.04)	00000 (± 00000)		
Physical Functioning, Week 156 (n=7, 0)	-4.76 (± 10.69)	00000 (± 00000)		
Physical Functioning, Week 165 (n=8, 0)	-3.61 (± 13.44)	00000 (± 00000)		
Physical Functioning, Week 174 (n=7, 0)	-1.90 (± 21.33)	00000 (± 00000)		
Physical Functioning, Week 183 (n=5, 0)	2.67 (± 19.21)	00000 (± 00000)		
Physical Functioning, Week 192 (n=4, 0)	-3.33 (± 12.77)	00000 (± 00000)		
Physical Functioning, Week 201	-3.33 (± 4.71)	00000 (± 00000)		
Physical Functioning, Week 210 (n=2, 0)	-20.00 (± 99999)	00000 (± 00000)		
Physical Functioning, SFUV (n=1, 0)	-9.70 (± 25.01)	-6.67 (± 27.08)		
Role Functioning, Baseline (n=294, 145)	62.53 (± 33.17)	61.72 (± 34.31)		
Role Functioning, Week 6 (n=222, 114)	-2.63 (± 28.13)	-3.51 (± 30.12)		
Role Functioning, Week 12 (n=150, 63)	-1.78 (± 30.48)	-1.59 (± 26.56)		
Role Functioning, Week 18 (n=122, 39)	-0.96 (± 30.02)	1.71 (± 36.63)		
Role Functioning, Week 24 (n=107, 30)	1.25 (± 30.00)	-5.00 (± 28.42)		
Role Functioning, Week 30 (n=84, 23)	-0.20 (± 29.10)	-7.25 (± 32.50)		
Role Functioning, Week 36 (n=62, 16)	2.15 (± 35.00)	-14.58 (± 47.09)		
Role Functioning, Week 42 (n=54, 14)	1.54 (± 35.95)	-4.76 (± 47.78)		

Role Functioning, Week 48 (n=44, 12)	4.92 (± 29.55)	-2.78 (± 34.69)		
Role Functioning, Week 57 (n=37, 8)	3.15 (± 28.82)	-4.17 (± 19.42)		
Role Functioning, Week 66 (n=33, 5)	0.51 (± 25.17)	-6.67 (± 25.28)		
Role Functioning, Week 75 (n=26, 4)	-0.64 (± 31.44)	8.33 (± 48.11)		
Role Functioning, Week 84 (n=18, 3)	3.70 (± 16.72)	-11.11 (± 19.25)		
Role Functioning, Week 93 (n=20, 2)	-1.67 (± 26.98)	-25.00 (± 35.36)		
Role Functioning, Week 102 (n=16, 1)	2.08 (± 18.13)	-33.33 (± 99999)		
Role Functioning, Week 111 (n=14, 0)	-3.57 (± 22.81)	00000 (± 00000)		
Role Functioning, Week 120 (n=14, 0)	-1.19 (± 19.02)	00000 (± 00000)		
Role Functioning, Week 129 (n=14, 0)	-1.19 (± 17.86)	00000 (± 00000)		
Role Functioning, Week 138 (n=14, 0)	-2.38 (± 22.51)	00000 (± 00000)		
Role Functioning, Week 147 (n=14, 0)	-3.57 (± 17.52)	00000 (± 00000)		
Role Functioning, Week 156 (n=7, 0)	-2.38 (± 6.30)	00000 (± 00000)		
Role Functioning, Week 165 (n=8, 0)	-10.42 (± 26.63)	00000 (± 00000)		
Role Functioning, Week 174 (n=7, 0)	-7.14 (± 26.97)	00000 (± 00000)		
Role Functioning, Week 183 (n=5, 0)	-10.00 (± 9.13)	00000 (± 00000)		
Role Functioning, Week 192 (n=4, 0)	-16.67 (± 13.61)	00000 (± 00000)		
Role Functioning, Week 201 (n=2, 0)	0.00 (± 0.00)	00000 (± 00000)		
Role Functioning, Week 210 (n=1, 0)	0.00 (± 99999)	00000 (± 00000)		
Role Functioning, SFUV (n=11, 13)	-22.73 (± 41.01)	-1.28 (± 43.28)		
Emotional Functioning, Baseline (n=290, 146)	74.20 (± 23.87)	73.38 (± 23.55)		
Emotional Functioning, Week 6 (n=219, 115)	2.12 (± 20.59)	0.46 (± 23.00)		
Emotional Functioning, Week 12 (n=148, 64)	1.24 (± 21.06)	4.21 (± 22.77)		
Emotional Functioning, Week 18 (n=120, 40)	3.82 (± 18.23)	0.28 (± 22.10)		
Emotional Functioning, Week 24 (n=105, 30)	4.13 (± 17.07)	4.07 (± 17.40)		
Emotional Functioning, Week 30 (n=83, 23)	3.15 (± 17.62)	2.17 (± 20.29)		
Emotional Functioning, Week 36 (n=62, 16)	2.02 (± 16.78)	-5.38 (± 21.31)		
Emotional Functioning, Week 42 (n=54, 14)	2.01 (± 19.08)	-7.14 (± 16.30)		
Emotional Functioning, Week 48 (n=43, 12)	5.04 (± 13.87)	-3.47 (± 10.33)		
Emotional Functioning, Week 57 (n=37, 8)	5.78 (± 20.58)	3.13 (± 23.12)		
Emotional Functioning, Week 66 (n=33, 5)	4.29 (± 17.81)	6.67 (± 6.97)		

Emotional Functioning, Week 75 (n=26, 4)	0.32 (± 21.01)	12.50 (± 28.46)		
Emotional Functioning, Week 84 (n=19, 3)	6.58 (± 17.91)	0.00 (± 16.97)		
Emotional Functioning, Week 93 (n=20, 2)	2.92 (± 13.59)	-4.17 (± 5.89)		
Emotional Functioning, Week 102 (n=16, 1)	4.69 (± 12.53)	-16.67 (± 99999)		
Emotional Functioning, Week 111 (n=14, 0)	3.57 (± 15.92)	00000 (± 00000)		
Emotional Functioning, Week 120 (n=14, 0)	1.79 (± 10.93)	00000 (± 00000)		
Emotional Functioning, Week 129 (n=14, 0)	2.98 (± 12.91)	00000 (± 00000)		
Emotional Functioning, Week 138 (n=14, 0)	4.17 (± 12.97)	00000 (± 00000)		
Emotional Functioning, Week 147 (n=14, 0)	5.36 (± 18.08)	00000 (± 00000)		
Emotional Functioning, Week 156 (n=7, 0)	2.38 (± 10.45)	00000 (± 00000)		
Emotional Functioning, Week 165 (n=8, 0)	-1.04 (± 8.26)	00000 (± 00000)		
Emotional Functioning, Week 174 (n=7, 0)	2.38 (± 12.47)	00000 (± 00000)		
Emotional Functioning, Week 183 (n=5, 0)	-1.67 (± 10.87)	00000 (± 00000)		
Emotional Functioning, Week 192 (n=4, 0)	-2.08 (± 10.49)	00000 (± 00000)		
Emotional Functioning, Week 201 (n=2, 0)	-4.17 (± 17.68)	00000 (± 00000)		
Emotional Functioning, Week 210 (n=1, 0)	-16.67 (± 99999)	00000 (± 00000)		
Emotional Functioning, SFUV (n=11, 13)	6.82 (± 26.57)	-5.77 (± 21.08)		
Cognitive Functioning, Baseline (n=291, 146)	81.39 (± 21.49)	82.65 (± 19.95)		
Cognitive Functioning, Week 6 (n=219, 115)	-1.67 (± 21.17)	-5.94 (± 21.76)		
Cognitive Functioning, Week 12 (n=149, 64)	-1.79 (± 22.52)	-2.60 (± 22.27)		
Cognitive Functioning, Week 18 (n=121, 40)	2.62 (± 19.95)	-7.92 (± 24.46)		
Cognitive Functioning, Week 24 (n=105, 30)	0.48 (± 18.41)	-10.00 (± 28.57)		
Cognitive Functioning, Week 30 (n=83, 23)	-2.01 (± 18.11)	-8.70 (± 17.31)		
Cognitive Functioning, Week 36 (n=62, 16)	-0.54 (± 15.96)	-11.46 (± 16.91)		
Cognitive Functioning, Week 42 (n=54, 14)	-4.94 (± 23.71)	-7.14 (± 12.60)		
Cognitive Functioning, Week 48 (n=44, 12)	-1.89 (± 16.16)	-11.11 (± 14.79)		
Cognitive Functioning, Week 57 (n=37, 8)	-3.15 (± 20.73)	-2.08 (± 16.52)		
Cognitive Functioning, Week 66 (n=33, 5)	-4.04 (± 23.58)	-3.33 (± 18.26)		
Cognitive Functioning, Week 75 (n=26, 4)	-5.13 (± 17.49)	-4.17 (± 20.97)		
Cognitive Functioning, Week 84 (n=19, 3)	-3.51 (± 18.90)	5.56 (± 9.62)		
Cognitive Functioning, Week 93 (n=20, 2)	3.33 (± 12.80)	0.00 (± 0.00)		

Cognitive Functioning, Week 102 (n=16, 1)	4.17 (± 16.67)	0.00 (± 99999)		
Cognitive Functioning, Week 111 (n=14, 0)	4.76 (± 16.57)	00000 (± 00000)		
Cognitive Functioning, Week 120 (n=14, 0)	0.00 (± 20.67)	00000 (± 00000)		
Cognitive Functioning, Week 129 (n=14, 0)	0.00 (± 13.07)	00000 (± 00000)		
Cognitive Functioning, Week 138 (n=14, 0)	-2.38 (± 20.52)	00000 (± 00000)		
Cognitive Functioning, Week 147 (n=14, 0)	1.19 (± 16.62)	00000 (± 00000)		
Cognitive Functioning, Week 156 (n=7, 0)	4.76 (± 12.60)	00000 (± 00000)		
Cognitive Functioning, Week 165 (n=8, 0)	6.25 (± 12.40)	00000 (± 00000)		
Cognitive Functioning, Week 174 (n=7, 0)	0.00 (± 9.62)	00000 (± 00000)		
Cognitive Functioning, Week 183 (n=5, 0)	3.33 (± 18.26)	00000 (± 00000)		
Cognitive Functioning, Week 192 (n=4, 0)	0.00 (± 0.00)	00000 (± 00000)		
Cognitive Functioning, Week 201 (n=2, 0)	0.00 (± 0.00)	00000 (± 00000)		
Cognitive Functioning, Week 210 (n=1, 0)	0.00 (± 99999)	00000 (± 00000)		
Cognitive Functioning, SFUV (n=11, 13)	-16.67 (± 23.57)	5.13 (± 25.81)		
Social Functioning, Baseline (n=290, 146)	71.32 (± 29.12)	74.43 (± 27.62)		
Social Functioning, Week 6 (n=218, 115)	1.30 (± 27.66)	-4.49 (± 28.30)		
Social Functioning, Week 12 (n=148, 64)	1.58 (± 27.93)	-4.17 (± 32.93)		
Social Functioning, Week 18 (n=119, 40)	5.60 (± 24.38)	-14.17 (± 31.93)		
Social Functioning, Week 24 (n=105, 30)	5.08 (± 24.91)	-11.11 (± 27.45)		
Social Functioning, Week 30 (n=83, 23)	4.82 (± 23.79)	-5.80 (± 36.10)		
Social Functioning, Week 36 (n=61, 16)	3.01 (± 27.97)	-14.58 (± 42.11)		
Social Functioning, Week 42 (n=54, 14)	-0.31 (± 26.79)	-7.14 (± 36.23)		
Social Functioning, Week 48 (n=44, 12)	1.89 (± 21.93)	-5.56 (± 28.72)		
Social Functioning, Week 57 (n=37, 8)	3.60 (± 29.17)	2.08 (± 30.13)		
Social Functioning, Week 66 (n=33, 5)	5.56 (± 26.90)	3.33 (± 29.81)		
Social Functioning, Week 75 (n=26, 4)	5.77 (± 23.07)	4.17 (± 34.36)		
Social Functioning, Week 84 (n=19, 3)	2.63 (± 21.70)	22.22 (± 25.46)		
Social Functioning, Week 93 (n=20, 2)	8.33 (± 16.67)	8.33 (± 11.79)		
Social Functioning, Week 102 (n=16, 1)	9.38 (± 17.18)	16.67 (± 99999)		
Social Functioning, Week 111 (n=14, 0)	2.38 (± 18.32)	00000 (± 00000)		
Social Functioning, Week 120 (n=14, 0)	7.14 (± 14.19)	00000 (± 00000)		
Social Functioning, Week 129 (n=14, 0)	-2.38 (± 30.56)	00000 (± 00000)		

Social Functioning, Week 138 (n=14, 0)	2.38 (± 20.52)	00000 (± 00000)		
Social Functioning, Week 147 (n=14, 0)	7.14 (± 16.94)	00000 (± 00000)		
Social Functioning, Week 156 (n=7, 0)	4.76 (± 15.85)	00000 (± 00000)		
Social Functioning, Week 165 (n=8, 0)	-6.25 (± 29.46)	00000 (± 00000)		
Social Functioning, Week 174 (n=7, 0)	7.14 (± 26.97)	00000 (± 00000)		
Social Functioning, Week 183 (n=5, 0)	6.67 (± 38.37)	00000 (± 00000)		
Social Functioning, Week 192 (n=4, 0)	-4.17 (± 28.46)	00000 (± 00000)		
Social Functioning, Week 201 (n=2, 0)	-25.00 (± 35.36)	00000 (± 00000)		
Social Functioning, Week 210 (n=1, 0)	-50.00 (± 99999)	00000 (± 00000)		
Social Functioning, SFUV (n=11, 13)	1.52 (± 46.22)	-12.82 (± 34.80)		
Fatigue, Baseline (n=293, 146)	41.62 (± 26.98)	42.62 (± 25.10)		
Fatigue, Week 6 (n=221, 115)	3.37 (± 23.32)	2.08 (± 23.71)		
Fatigue, Week 12 (n=148, 64)	0.53 (± 26.98)	-1.56 (± 22.99)		
Fatigue, Week 18 (n=121, 40)	-1.79 (± 22.11)	2.22 (± 18.69)		
Fatigue, Week 24 (n=106, 30)	-3.14 (± 25.82)	2.96 (± 21.43)		
Fatigue, Week 30 (n=83, 23)	-2.88 (± 22.98)	-3.38 (± 24.03)		
Fatigue, Week 36 (n=63, 16)	-4.06 (± 28.12)	4.86 (± 27.81)		
Fatigue, Week 42 (n=54, 14)	-2.67 (± 29.11)	3.17 (± 28.05)		
Fatigue, Week 48 (n=43, 12)	-6.72 (± 24.86)	1.85 (± 23.61)		
Fatigue, Week 57 (n=37, 8)	-3.30 (± 22.66)	1.39 (± 18.25)		
Fatigue, Week 66 (n=33, 5)	-2.53 (± 29.63)	-6.67 (± 12.67)		
Fatigue, Week 75 (n=26, 4)	-4.70 (± 22.26)	-8.33 (± 33.18)		
Fatigue, Week 84 (n=18, 3)	-6.79 (± 26.72)	22.22 (± 19.25)		
Fatigue, Week 93 (n=20, 2)	-5.56 (± 30.05)	22.22 (± 0.00)		
Fatigue, Week 102 (n=16, 1)	-5.56 (± 26.91)	33.33 (± 99999)		
Fatigue, Week 111 (n=14, 0)	-0.79 (± 33.32)	00000 (± 00000)		
Fatigue, Week 120 (n=14, 0)	-2.38 (± 28.30)	00000 (± 00000)		
Fatigue, Week 129 (n=14, 0)	-2.78 (± 18.33)	00000 (± 00000)		
Fatigue, Week 138 (n=14, 0)	-1.59 (± 26.10)	00000 (± 00000)		
Fatigue, Week 147 (n=14, 0)	-3.17 (± 25.94)	00000 (± 00000)		
Fatigue, Week 156 (n=7, 0)	-1.59 (± 14.95)	00000 (± 00000)		

Fatigue, Week 165 (n=8, 0)	1.39 (± 29.95)	00000 (± 00000)		
Fatigue, Week 174 (n=7, 0)	-4.76 (± 20.14)	00000 (± 00000)		
Fatigue, Week 183 (n=5, 0)	4.44 (± 26.76)	00000 (± 00000)		
Fatigue, Week 192 (n=4, 0)	5.56 (± 14.34)	00000 (± 00000)		
Fatigue, Week 201 (n=2, 0)	-5.56 (± 7.86)	00000 (± 00000)		
Fatigue, Week 210 (n=1, 0)	-11.11 (± 99999)	00000 (± 00000)		
Fatigue, SFUV (n=11, 13)	0.00 (± 31.82)	1.71 (± 33.59)		
Nausea and Vomiting, Baseline (n=294, 146)	8.28 (± 17.07)	7.99 (± 15.06)		
Nausea and Vomiting, Week 6 (n=222, 115)	0.90 (± 16.98)	1.01 (± 19.28)		
Nausea and Vomiting, Week 12 (n=149, 64)	1.12 (± 17.72)	3.65 (± 16.92)		
Nausea and Vomiting, Week 18 (n=122, 40)	-0.41 (± 15.67)	3.33 (± 18.18)		
Nausea and Vomiting, Week 24 (n=107, 30)	-1.87 (± 14.54)	3.33 (± 16.02)		
Nausea and Vomiting, Week 30 (n=84, 23)	-2.38 (± 16.39)	3.62 (± 10.0063)		
Nausea and Vomiting, Week 36 (n=63, 16)	2.12 (± 17.32)	3.13 (± 15.18)		
Nausea and Vomiting, Week 42 (n=54, 14)	1.54 (± 11.79)	3.57 (± 19.81)		
Nausea and Vomiting, Week 48 (n=43, 12)	-1.55 (± 15.78)	0.00 (± 20.10)		
Nausea and Vomiting, Week 57 (n=37, 8)	2.25 (± 11.89)	2.08 (± 18.77)		
Nausea and Vomiting, Week 66 (n=33, 5)	-1.01 (± 14.99)	-3.33 (± 7.45)		
Nausea and Vomiting, Week 75 (n=26, 4)	2.56 (± 9.06)	-4.17 (± 8.33)		
Nausea and Vomiting, Week 84 (n=19, 3)	0.88 (± 8.74)	0.00 (± 16.67)		
Nausea and Vomiting, Week 93 (n=20, 2)	-1.67 (± 5.13)	-8.33 (± 11.79)		
Nausea and Vomiting, Week 102 (n=16, 1)	-2.08 (± 5.69)	0.00 (± 99999)		
Nausea and Vomiting, Week 111 (n=14, 0)	4.76 (± 12.10)	00000 (± 00000)		
Nausea and Vomiting, Week 120 (n=14, 0)	-1.19 (± 7.91)	00000 (± 00000)		
Nausea and Vomiting, Week 129 (n=14, 0)	0.00 (± 6.54)	00000 (± 00000)		
Nausea and Vomiting, Week 138 (n=14, 0)	-2.38 (± 6.05)	00000 (± 00000)		
Nausea and Vomiting, Week 147 (n=14, 0)	-2.38 (± 6.05)	00000 (± 00000)		
Nausea and Vomiting, Week 156 (n=7, 0)	-2.38 (± 6.30)	00000 (± 00000)		
Nausea and Vomiting, Week 165 (n=8, 0)	-2.08 (± 5.89)	00000 (± 00000)		
Nausea and Vomiting, Week 174 (n=7, 0)	-2.38 (± 6.30)	00000 (± 00000)		
Nausea and Vomiting, Week 183 (n=5, 0)	-3.33 (± 7.45)	00000 (± 00000)		

Nausea and Vomiting, Week 192 (n=4, 0)	0.00 (± 0.00)	00000 (± 00000)		
Nausea and Vomiting, Week 201 (n=2, 0)	0.00 (± 0.00)	00000 (± 00000)		
Nausea and Vomiting, Week 210 (n=1, 0)	0.00 (± 99999)	00000 (± 00000)		
Nausea and Vomiting, SFUV (n=11, 13)	13.64 (± 42.04)	0.00 (± 33.33)		
Pain, Baseline (n=294, 146)	31.52 (± 29.67)	32.99 (± 29.06)		
Pain, Week 6 (n=222, 115)	-0.98 (± 25.27)	-1.01 (± 26.61)		
Pain, Week 12 (n=149, 64)	-3.58 (± 29.67)	-5.73 (± 27.09)		
Pain, Week 18 (n=121, 40)	-5.51 (± 30.38)	3.75 (± 31.23)		
Pain, Week 24 (n=107, 30)	-6.70 (± 30.01)	3.89 (± 23.44)		
Pain, Week 30 (n=84, 23)	-5.36 (± 30.30)	-9.42 (± 21.80)		
Pain, Week 36 (n=63, 16)	-7.41 (± 28.36)	3.13 (± 25.25)		
Pain, Week 42 (n=54, 14)	-5.25 (± 33.77)	-4.76 (± 33.61)		
Pain, Week 48 (n=44, 12)	-9.85 (± 30.57)	-11.11 (± 26.91)		
Pain, Week 57 (n=37, 8)	-7.21 (± 31.80)	-6.25 (± 25.10)		
Pain, Week 66 (n=33, 5)	-13.13 (± 30.26)	-20.00 (± 21.73)		
Pain, Week 75 (n=26, 4)	-5.77 (± 33.65)	0.00 (± 36.00)		
Pain, Week 84 (n=19, 3)	-15.79 (± 26.34)	-11.11 (± 19.25)		
Pain, Week 93 (n=20, 2)	-7.50 (± 27.29)	-16.67 (± 23.57)		
Pain, Week 102 (n=16, 1)	-17.71 (± 25.44)	-33.33 (± 99999)		
Pain, Week 111 (n=14, 0)	-14.29 (± 23.44)	00000 (± 00000)		
Pain, Week 120 (n=14, 0)	-15.48 (± 26.53)	00000 (± 00000)		
Pain, Week 129 (n=14, 0)	-10.71 (± 16.80)	00000 (± 00000)		
Pain, Week 138 (n=14, 0)	-15.48 (± 25.71)	00000 (± 00000)		
Pain, Week 147 (n=14, 0)	-13.10 (± 27.87)	00000 (± 00000)		
Pain, Week 156 (n=7, 0)	-14.29 (± 20.25)	00000 (± 00000)		
Pain, Week 165 (n=8, 0)	-10.42 (± 19.80)	00000 (± 00000)		
Pain, Week 174 (n=7, 0)	-11.90 (± 34.31)	00000 (± 00000)		
Pain, Week 183 (n=5, 0)	-13.33 (± 36.13)	00000 (± 00000)		
Pain, Week 192 (n=4, 0)	-12.50 (± 25.00)	00000 (± 00000)		
Pain, Week 201 (n=2, 0)	-25.00 (± 35.36)	00000 (± 00000)		
Pain, Week 210 (n=1, 0)	-16.67 (± 99999)	00000 (± 00000)		

Pain, SFUV (n=11, 13)	9.09 (± 26.21)	-7.69 (± 38.26)		
Dyspnoea, Baseline (n=294, 145)	36.17 (± 30.47)	39.31 (± 31.35)		
Dyspnoea, Week 6 (n=220, 114)	-1.36 (± 28.55)	-0.58 (± 29.74)		
Dyspnoea, Week 12 (n=149, 64)	0.45 (± 30.51)	-4.69 (± 27.13)		
Dyspnoea, Week 18 (n=122, 40)	-1.91 (± 26.87)	-3.33 (± 31.85)		
Dyspnoea, Week 24 (n=106, 30)	-5.03 (± 29.02)	-4.44 (± 29.99)		
Dyspnoea, Week 30 (n=84, 23)	-4.37 (± 28.24)	-8.70 (± 30.51)		
Dyspnoea, Week 36 (n=62, 16)	-6.99 (± 27.08)	0.00 (± 34.43)		
Dyspnoea, Week 42 (n=54, 13)	-8.64 (± 32.50)	-7.69 (± 19.97)		
Dyspnoea, Week 48 (n=44, 11)	-7.58 (± 30.38)	-3.03 (± 23.35)		
Dyspnoea, Week 57 (n=37, 8)	-9.01 (± 30.07)	-12.50 (± 24.80)		
Dyspnoea, Week 66 (n=33, 5)	-3.03 (± 30.46)	-20.00 (± 18.26)		
Dyspnoea, Week 75 (n=26, 4)	-5.13 (± 22.49)	-16.67 (± 19.25)		
Dyspnoea, Week 84 (n=18, 3)	-9.26 (± 25.06)	0.00 (± 0.00)		
Dyspnoea, Week 93 (n=20, 2)	0.00 (± 35.87)	-16.67 (± 23.57)		
Dyspnoea, Week 102 (n=16, 1)	4.17 (± 26.87)	0.00 (± 99999)		
Dyspnoea, Week 111 (n=13, 0)	-7.69 (± 33.76)	00000 (± 00000)		
Dyspnoea, Week 120 (n=14, 0)	0.00 (± 22.65)	00000 (± 00000)		
Dyspnoea, Week 129 (n=14, 0)	2.38 (± 24.33)	00000 (± 00000)		
Dyspnoea, Week 138 (n=14, 0)	-2.38 (± 27.62)	00000 (± 00000)		
Dyspnoea, Week 147 (n=14, 0)	-4.76 (± 22.10)	00000 (± 00000)		
Dyspnoea, Week 156 (n=7, 0)	0.00 (± 19.25)	00000 (± 00000)		
Dyspnoea, Week 165 (n=8, 0)	-4.17 (± 21.36)	00000 (± 00000)		
Dyspnoea, Week 174 (n=7, 0)	4.76 (± 23.00)	00000 (± 00000)		
Dyspnoea, Week 183 (n=5, 0)	6.67 (± 27.89)	00000 (± 00000)		
Dyspnoea, Week 192 (n=4, 0)	0.00 (± 27.22)	00000 (± 00000)		
Dyspnoea, Week 201 (n=1, 0)	0.00 (± 99999)	00000 (± 00000)		
Dyspnoea, Week 210 (n=1, 0)	0.00 (± 99999)	00000 (± 00000)		
Dyspnoea, SFUV (n=11, 12)	24.24 (± 44.95)	-2.78 (± 43.71)		
Insomnia, Baseline (n=294, 146)	30.50 (± 29.97)	31.05 (± 32.44)		
Insomnia, Week 6 (n=222, 115)	-1.95 (± 31.25)	-1.16 (± 33.60)		

Insomnia, Week 12 (n=150, 64)	-1.78 (± 31.32)	-3.65 (± 33.13)		
Insomnia, Week 18 (n=122, 40)	-4.37 (± 27.76)	-2.50 (± 36.51)		
Insomnia, Week 24 (n=107, 30)	-6.23 (± 29.01)	-5.56 (± 31.66)		
Insomnia, Week 30 (n=84, 23)	-3.17 (± 26.19)	-15.94 (± 28.19)		
Insomnia, Week 36 (n=63, 16)	-3.17 (± 26.58)	-18.75 (± 34.36)		
Insomnia, Week 42 (n=54, 14)	-3.09 (± 36.21)	-9.52 (± 27.51)		
Insomnia, Week 48 (n=43, 12)	-6.20 (± 27.46)	2.78 (± 26.43)		
Insomnia, Week 57 (n=37, 8)	-9.91 (± 32.27)	4.17 (± 33.03)		
Insomnia, Week 66 (n=33, 5)	-8.08 (± 27.68)	-6.67 (± 14.91)		
Insomnia, Week 75 (n=26, 4)	-8.97 (± 27.58)	-16.67 (± 19.25)		
Insomnia, Week 84 (n=18, 3)	-7.41 (± 24.40)	-22.22 (± 19.25)		
Insomnia, Week 93 (n=20, 2)	-8.33 (± 23.88)	0.00 (± 0.00)		
Insomnia, Week 102 (n=16, 1)	-10.42 (± 20.07)	0.00 (± 99999)		
Insomnia, Week 111 (n=14, 0)	-9.52 (± 20.37)	00000 (± 00000)		
Insomnia, Week 120 (n=14, 0)	-11.90 (± 21.11)	00000 (± 00000)		
Insomnia, Week 129 (n=14, 0)	-9.52 (± 20.37)	00000 (± 00000)		
Insomnia, Week 138 (n=14, 0)	-16.67 (± 21.68)	00000 (± 00000)		
Insomnia, Week 147 (n=14, 0)	-14.29 (± 28.39)	00000 (± 00000)		
Insomnia, Week 156 (n=7, 0)	-4.76 (± 12.60)	00000 (± 00000)		
Insomnia, Week 165 (n=8, 0)	0.00 (± 17.82)	00000 (± 00000)		
Insomnia, Week 174 (n=7, 0)	-9.52 (± 16.27)	00000 (± 00000)		
Insomnia, Week 183 (n=5, 0)	-13.33 (± 38.01)	00000 (± 00000)		
Insomnia, Week 192 (n=4, 0)	-8.33 (± 16.67)	00000 (± 00000)		
Insomnia, Week 201 (n=2, 0)	-33.33 (± 47.14)	00000 (± 00000)		
Insomnia, Week 210 (n=1, 0)	-33.33 (± 99999)	00000 (± 00000)		
Insomnia, SFUV (n=11, 13)	12.12 (± 42.88)	-5.13 (± 35.61)		
Appetite Loss, Baseline (n=294, 146)	31.63 (± 33.06)	31.05 (± 32.91)		
Appetite Loss, Week 6 (n=221, 114)	1.06 (± 33.99)	0.00 (± 38.40)		
Appetite Loss, Week 12 (n=150, 64)	-4.22 (± 35.46)	7.29 (± 32.24)		
Appetite Loss, Week 18 (n=122, 40)	-7.38 (± 33.06)	13.33 (± 27.01)		
Appetite Loss, Week 24 (n=106, 30)	-9.43 (± 28.27)	10.00 (± 32.93)		

Appetite Loss, Week 30 (n=84, 23)	-12.30 (± 28.24)	7.25 (± 31.71)		
Appetite Loss, Week 36 (n=63, 16)	-11.11 (± 33.87)	6.25 (± 30.35)		
Appetite Loss, Week 42 (n=54, 14)	-7.41 (± 32.81)	2.38 (± 27.62)		
Appetite Loss, Week 48 (n=43, 12)	-10.85 (± 29.74)	5.56 (± 44.57)		
Appetite Loss, Week 57 (n=37, 8)	-6.31 (± 31.27)	8.33 (± 42.72)		
Appetite Loss, Week 66 (n=33, 5)	-9.09 (± 29.19)	13.33 (± 29.81)		
Appetite Loss, Week 75 (n=26, 4)	-10.26 (± 30.94)	0.00 (± 27.22)		
Appetite Loss, Week 84 (n=19, 3)	-17.54 (± 28.04)	22.22 (± 19.25)		
Appetite Loss, Week 93 (n=20, 2)	-10.00 (± 26.71)	50.00 (± 23.57)		
Appetite Loss, Week 102 (n=16, 1)	-10.42 (± 20.07)	66.67 (± 99999)		
Appetite Loss, Week 111 (n=14, 0)	-7.14 (± 23.31)	00000 (± 00000)		
Appetite Loss, Week 120 (n=14, 0)	-9.52 (± 27.51)	00000 (± 00000)		
Appetite Loss, Week 129 (n=14, 0)	-7.14 (± 23.31)	00000 (± 00000)		
Appetite Loss, Week 138 (n=14, 0)	-9.52 (± 24.21)	00000 (± 00000)		
Appetite Loss, Week 147 (n=14, 0)	-16.67 (± 31.35)	00000 (± 00000)		
Appetite Loss, Week 156 (n=7, 0)	0.00 (± 0.00)	00000 (± 00000)		
Appetite Loss, Week 165 (n=8, 0)	0.00 (± 0.00)	00000 (± 00000)		
Appetite Loss, Week 174 (n=7, 0)	-9.52 (± 25.20)	00000 (± 00000)		
Appetite Loss, Week 183 (n=5, 0)	-13.33 (± 29.81)	00000 (± 00000)		
Appetite Loss, Week 192 (n=4, 0)	8.33 (± 16.67)	00000 (± 00000)		
Appetite Loss, Week 201 (n=2, 0)	16.67 (± 23.57)	00000 (± 00000)		
Appetite Loss, Week 210 (n=1, 0)	0.00 (± 99999)	00000 (± 00000)		
Appetite Loss, SFUV (n=11, 13)	-9.09 (± 39.70)	-7.69 (± 52.97)		
Constipation, Baseline (n=294, 146)	21.20 (± 30.67)	21.92 (± 27.80)		
Constipation, Week 6 (n=221, 115)	-0.45 (± 27.98)	1.45 (± 31.65)		
Constipation, Week 12 (n=149, 64)	-2.46 (± 29.79)	-0.52 (± 28.17)		
Constipation, Week 18 (n=122, 40)	-6.01 (± 29.39)	0.83 (± 29.71)		
Constipation, Week 24 (n=107, 30)	-5.61 (± 29.13)	1.11 (± 22.29)		
Constipation, Week 30 (n=84, 23)	-6.75 (± 27.76)	5.80 (± 25.92)		
Constipation, Week 36 (n=63, 16)	-7.94 (± 33.18)	6.25 (± 18.13)		
Constipation, Week 42 (n=54, 14)	-4.94 (± 31.33)	0.00 (± 18.49)		

Constipation, Week 48 (n=44, 11)	-10.61 (± 32.76)	-6.06 (± 25.03)		
Constipation, Week 57 (n=37, 8)	-15.32 (± 28.97)	-8.33 (± 15.43)		
Constipation, Week 66 (n=33, 5)	-13.13 (± 27.56)	0.00 (± 23.57)		
Constipation, Week 75 (n=26, 4)	-5.13 (± 32.24)	16.67 (± 57.74)		
Constipation, Week 84 (n=19, 3)	-3.51 (± 31.22)	11.11 (± 38.49)		
Constipation, Week 93 (n=20, 2)	-8.33 (± 35.66)	33.33 (± 0.00)		
Constipation, Week 102 (n=16, 1)	-10.42 (± 35.94)	33.33 (± 99999)		
Constipation, Week 111 (n=14, 0)	-7.14 (± 41.71)	00000 (± 00000)		
Constipation, Week 120 (n=14, 0)	-4.76 (± 41.05)	00000 (± 00000)		
Constipation, Week 129 (n=14, 0)	-7.14 (± 41.71)	00000 (± 00000)		
Constipation, Week 138 (n=14, 0)	-9.52 (± 47.91)	00000 (± 00000)		
Constipation, Week 147 (n=14, 0)	-11.90 (± 42.58)	00000 (± 00000)		
Constipation, Week 156 (n=7, 0)	-14.29 (± 26.23)	00000 (± 00000)		
Constipation, Week 165 (n=8, 0)	-8.33 (± 29.55)	00000 (± 00000)		
Constipation, Week 174 (n=7, 0)	-14.29 (± 26.23)	00000 (± 00000)		
Constipation, Week 183 (n=5, 0)	-13.33 (± 18.26)	00000 (± 00000)		
Constipation, Week 192 (n=4, 0)	0.00 (± 27.22)	00000 (± 00000)		
Constipation, Week 201 (n=2, 0)	16.67 (± 23.57)	00000 (± 00000)		
Constipation, Week 210 (n=1, 0)	0.00 (± 99999)	00000 (± 00000)		
Constipation, SFUV (n=11, 13)	3.03 (± 45.84)	7.69 (± 30.89)		
Diarrhoea, Baseline (n=290, 146)	5.63 (± 15.28)	5.71 (± 16.31)		
Diarrhoea, Week 6 (n=219, 115)	-0.61 (± 19.93)	3.48 (± 23.93)		
Diarrhoea, Week 12 (n=148, 63)	1.80 (± 21.57)	1.06 (± 18.90)		
Diarrhoea, Week 18 (n=120, 40)	-0.83 (± 18.57)	5.83 (± 24.91)		
Diarrhoea, Week 24 (n=104, 30)	0.00 (± 18.58)	5.56 (± 17.69)		
Diarrhoea, Week 30 (n=83, 23)	2.01 (± 19.02)	4.35 (± 11.48)		
Diarrhoea, Week 36 (n=62, 16)	0.00 (± 20.91)	2.08 (± 8.33)		
Diarrhoea, Week 42 (n=54, 14)	-3.09 (± 17.46)	2.38 (± 8.91)		
Diarrhoea, Week 48 (n=44, 12)	-0.76 (± 15.23)	8.33 (± 20.72)		
Diarrhoea, Week 57 (n=37, 8)	0.00 (± 20.79)	4.17 (± 11.79)		
Diarrhoea, Week 66 (n=33, 5)	-4.04 (± 18.18)	6.67 (± 14.91)		
Diarrhoea, Week 75 (n=26, 4)	-5.13 (± 15.47)	0.00 (± 0.00)		
Diarrhoea, Week 84 (n=19, 3)	1.75 (± 13.49)	0.00 (± 0.00)		
Diarrhoea, Week 93 (n=20, 2)	1.67 (± 25.31)	0.00 (± 0.00)		
Diarrhoea, Week 102 (n=16, 1)	0.00 (± 17.21)	0.00 (± 99999)		

Diarrhoea, Week 111 (n=14, 0)	7.14 (± 29.75)	00000 (± 00000)		
Diarrhoea, Week 120 (n=14, 0)	4.76 (± 34.24)	00000 (± 00000)		
Diarrhoea, Week 129 (n=14, 0)	2.38 (± 33.24)	00000 (± 00000)		
Diarrhoea, Week 138 (n=14, 0)	-4.76 (± 17.82)	00000 (± 00000)		
Diarrhoea, Week 147 (n=14, 0)	-4.76 (± 22.10)	00000 (± 00000)		
Diarrhoea, Week 156 (n=7, 0)	-4.76 (± 12.60)	00000 (± 00000)		
Diarrhoea, Week 165 (n=7, 0)	0.00 (± 0.00)	00000 (± 00000)		
Diarrhoea, Week 174 (n=7, 0)	-9.52 (± 25.20)	00000 (± 00000)		
Diarrhoea, Week 183 (n=5, 0)	-13.33 (± 29.81)	00000 (± 00000)		
Diarrhoea, Week 192 (n=4, 0)	0.00 (± 0.00)	00000 (± 00000)		
Diarrhoea, Week 201 (n=2, 0)	0.00 (± 0.00)	00000 (± 00000)		
Diarrhoea, Week 210 (n=1, 0)	0.00 (± 99999)	00000 (± 00000)		
Diarrhoea, SFUV (n=11, 13)	6.06 (± 29.13)	0.00 (± 13.61)		
Financial Difficulties, Baseline (n=291, 146)	22.22 (± 28.81)	20.32 (± 28.60)		
Financial Difficulties, Week 6 (n=219, 115)	-3.20 (± 27.00)	0.00 (± 25.74)		
Financial Difficulties, Week 12 (n=148, 64)	-4.95 (± 27.59)	1.56 (± 26.18)		
Financial Difficulties, Week 18 (n=121, 40)	-4.41 (± 23.94)	4.17 (± 27.41)		
Financial Difficulties, Week 24 (n=105, 30)	-4.76 (± 30.11)	2.22 (± 23.05)		
Financial Difficulties, Week 30 (n=83, 23)	-3.21 (± 24.20)	-1.45 (± 23.52)		
Financial Difficulties, Week 36 (n=62, 15)	-2.69 (± 28.50)	4.44 (± 21.33)		
Financial Difficulties, Week 42 (n=54, 14)	-1.85 (± 33.28)	2.38 (± 27.62)		
Financial Difficulties, Week 48 (n=44, 12)	-0.76 (± 29.19)	-5.56 (± 27.83)		
Financial Difficulties, Week 57 (n=37, 8)	-4.50 (± 32.55)	-4.17 (± 21.36)		
Financial Difficulties, Week 66 (n=33, 5)	0.00 (± 28.87)	-6.67 (± 27.89)		
Financial Difficulties, Week 75 (n=26, 4)	1.28 (± 29.03)	8.33 (± 31.91)		
Financial Difficulties, Week 84 (n=19, 3)	3.51 (± 26.98)	-22.22 (± 19.25)		
Financial Difficulties, Week 93 (n=20, 2)	0.00 (± 26.49)	-16.67 (± 23.57)		
Financial Difficulties, Week 102 (n=16, 1)	2.08 (± 25.73)	-33.33 (± 99999)		
Financial Difficulties, Week 111 (n=14, 0)	2.38 (± 27.62)	00000 (± 00000)		
Financial Difficulties, Week 120 (n=14, 0)	-2.38 (± 27.62)	00000 (± 00000)		
Financial Difficulties, Week 129 (n=14, 0)	-2.38 (± 24.33)	00000 (± 00000)		
Financial Difficulties, Week 138 (n=14, 0)	2.38 (± 30.56)	00000 (± 00000)		

Financial Difficulties, Week 147 (n=14, 0)	-2.38 (± 27.62)	00000 (± 00000)		
Financial Difficulties, Week 156 (n=7, 0)	-9.52 (± 31.71)	00000 (± 00000)		
Financial Difficulties, Week 165 (n=8, 0)	4.17 (± 37.53)	00000 (± 00000)		
Financial Difficulties, Week 174 (n=7, 0)	-9.52 (± 31.71)	00000 (± 00000)		
Financial Difficulties, Week 183 (n=5, 0)	0.00 (± 23.57)	00000 (± 00000)		
Financial Difficulties, Week 192 (n=4, 0)	0.00 (± 27.22)	00000 (± 00000)		
Financial Difficulties, Week 201 (n=2, 0)	16.67 (± 23.57)	00000 (± 00000)		
Financial Difficulties, Week 210 (n=1, 0)	0.00 (± 99999)	00000 (± 00000)		
Financial Difficulties, SFUV (n=11, 13)	-3.03 (± 43.34)	0.00 (± 27.22)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in EORTC QLQ Supplementary Lung Cancer Module 13 (EORTC QLQ-LC13) Score

End point title	Change From Baseline in EORTC QLQ Supplementary Lung Cancer Module 13 (EORTC QLQ-LC13) Score

End point description:

EORTC QLQ-LC13 module incorporates 1 multiple item scale to assess dyspnea &series of single items assessing pain,coughing,sore mouth,dysphagia, peripheral neuropathy,alopecia,& hemoptysis. It was scored according to EORTC scoring manual. All EORTC scales & single-item measures are linearly transformed so that each score has a range of 0-100. A high score for functional/global health status scale =high/healthy level of functioning/HRQoL (Health-Related Quality of Life); high score for symptom scale/item = high level of symptomatology/problems. A≥10-point change in the symptoms subscale score was perceived as clinically significant. '99999'=standard deviation (SD) non-estimable due to 1 participant evaluated. '00000'=data not reported due to no participant evaluated. ITT Population=all randomized participants irrespective of whether the assigned treatment was actually received. "n"=number of participants with data available for analysis at the specified timepoint.

End point type	Secondary

End point timeframe:

Baseline, Day 1 of each treatment cycle up to 30 days after last dose (up to approximately 55 months) (Cycle length = 21 days)

End point values	Atezolizumab	Single Agent Chemotherapy (Vinorelbine or Gemcitabine)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	302	151		
Units: units of a scale				
arithmetic mean (standard deviation)				
Dyspnoea, Baseline (n=287, 140)	34.30 (± 25.69)	36.67 (± 25.35)		
Dyspnoea, Week 6 (n=207, 109)	1.13 (± 19.90)	0.92 (± 24.25)		

Dyspnoea, Week 12 (n=144, 62)	-0.23 (± 24.28)	-2.87 (± 24.55)		
Dyspnoea, Week 18 (n=114, 37)	-4.78 (± 18.93)	0.90 (± 23.33)		
Dyspnoea, Week 24 (n=99, 29)	-5.05 (± 22.91)	2.68 (± 23.13)		
Dyspnoea, Week 30 (n=79, 22)	-5.34 (± 22.00)	1.52 (± 25.03)		
Dyspnoea, Week 36 (n=57, 14)	-3.90 (± 26.85)	5.56 (± 19.85)		
Dyspnoea, Week 42 (n=48, 13)	-11.11 (± 26.63)	-6.84 (± 22.01)		
Dyspnoea, Week 48 (n=39, 12)	-4.84 (± 26.83)	1.85 (± 22.64)		
Dyspnoea, Week 57 (n=31, 8)	-7.89 (± 20.53)	4.17 (± 15.64)		
Dyspnoea, Week 66 (n=27, 5)	-6.58 (± 24.12)	0.00 (± 13.61)		
Dyspnoea, Week 75 (n=22, 4)	-4.55 (± 23.67)	-2.78 (± 30.60)		
Dyspnoea, Week 84 (n=17, 3)	-8.50 (± 23.74)	3.70 (± 23.13)		
Dyspnoea, Week 93 (n=19, 2)	-2.34 (± 27.61)	5.56 (± 7.86)		
Dyspnoea, Week 102 (n=15, 1)	-2.96 (± 21.19)	0.00 (± 99999)		
Dyspnoea, Week 111 (n=13, 0)	-2.56 (± 26.51)	00000 (± 00000)		
Dyspnoea, Week 120 (n=13, 0)	-4.27 (± 24.23)	00000 (± 00000)		
Dyspnoea, Week 129 (n=12, 0)	3.70 (± 15.95)	00000 (± 00000)		
Dyspnoea, Week 138 (n=13, 0)	0.00 (± 24.43)	00000 (± 00000)		
Dyspnoea, Week 147 (n=13, 0)	-0.85 (± 26.24)	00000 (± 00000)		
Dyspnoea, Week 156 (n=7, 0)	1.59 (± 14.95)	00000 (± 00000)		
Dyspnoea, Week 165 (n=6, 0)	-1.85 (± 21.56)	00000 (± 00000)		
Dyspnoea, Week 174 (n=7, 0)	1.59 (± 17.48)	00000 (± 00000)		
Dyspnoea, Week 183 (n=4, 0)	5.56 (± 21.28)	00000 (± 00000)		
Dyspnoea, Week 192 (n=4, 0)	5.56 (± 26.45)	00000 (± 00000)		
Dyspnoea, Week 201 (n=2, 0)	0.00 (± 15.71)	00000 (± 00000)		
Dyspnoea, Week 210 (n=1, 0)	0.00 (± 99999)	00000 (± 00000)		
Dyspnoea, Safety Follow-Up Visit (n=11, 12)	12.12 (± 29.17)	6.48 (± 31.94)		
Coughing, Baseline (n=295, 147)	41.36 (± 30.24)	46.26 (± 28.25)		
Coughing, Week 6 (n=222, 116)	-1.80 (± 25.10)	-5.46 (± 29.80)		
Coughing, Week 12 (n=149, 64)	-7.61 (± 30.79)	-9.38 (± 29.97)		
Coughing, Week 18 (n=121, 39)	-9.64 (± 29.01)	-3.42 (± 34.87)		
Coughing, Week 24 (n=106, 30)	-11.01 (± 30.42)	3.33 (± 30.76)		

Coughing, Week 30 (n=83, 24)	-9.24 (± 33.46)	0.00 (± 26.01)		
Coughing, Week 36 (n=61, 16)	-7.10 (± 35.02)	0.00 (± 34.43)		
Coughing, Week 42 (n=53, 14)	-10.06 (± 31.07)	-2.38 (± 27.62)		
Coughing, Week 48 (n=44, 12)	-15.91 (± 30.06)	0.00 (± 20.10)		
Coughing, Week 57 (n=35, 8)	-14.29 (± 31.61)	4.17 (± 27.82)		
Coughing, Week 66 (n=32, 5)	-11.46 (± 33.45)	-13.33 (± 18.26)		
Coughing, Week 75 (n=25, 4)	-9.33 (± 28.09)	-8.33 (± 16.67)		
Coughing, Week 84 (n=19, 3)	-19.30 (± 32.04)	11.11 (± 19.25)		
Coughing, Week 93 (n=20, 2)	-21.67 (± 31.11)	16.67 (± 23.57)		
Coughing, Week 102 (n=16, 1)	-14.58 (± 20.97)	0.00 (± 99999)		
Coughing, Week 111 (n=14, 0)	-11.90 (± 21.11)	00000 (± 00000)		
Coughing, Week 120 (n=14, 0)	-11.90 (± 21.11)	00000 (± 00000)		
Coughing, Week 129 (n=14, 0)	-14.29 (± 21.54)	00000 (± 00000)		
Coughing, Week 138 (n=14, 0)	-16.67 (± 21.68)	00000 (± 00000)		
Coughing, Week 147 (n=14, 0)	-21.43 (± 24.83)	00000 (± 00000)		
Coughing, Week 156 (n=7, 0)	-23.81 (± 31.71)	00000 (± 00000)		
Coughing, Week 165 (n=8, 0)	-16.67 (± 35.63)	00000 (± 00000)		
Coughing, Week 174 (n=7, 0)	-19.05 (± 32.53)	00000 (± 00000)		
Coughing, Week 183 (n=4, 0)	0.00 (± 27.22)	00000 (± 00000)		
Coughing, Week 192 (n=4, 0)	-16.67 (± 19.25)	00000 (± 00000)		
Coughing, Week 201 (n=2, 0)	0.00 (± 0.00)	00000 (± 00000)		
Coughing, Week 210 (n=1, 0)	0.00 (± 99999)	00000 (± 00000)		
Coughing, Safety Follow-Up Visit (n=11, 13)	3.03 (± 37.87)	-17.95 (± 25.88)		
Haemoptysis, Baseline (n=296, 146)	5.86 (± 14.38)	7.76 (± 18.79)		
Haemoptysis, Week 6 (n=223, 115)	0.75 (± 19.10)	-4.64 (± 21.58)		
Haemoptysis, Week 12 (n=148, 63)	-1.80 (± 15.45)	-3.17 (± 20.49)		
Haemoptysis, Week 18 (n=122, 39)	-1.64 (± 15.95)	-1.71 (± 17.01)		
Haemoptysis, Week 24 (n=106, 30)	-2.52 (± 13.57)	-1.11 (± 18.54)		
Haemoptysis, Week 30 (n=84, 23)	-3.97 (± 14.08)	-2.90 (± 13.90)		
Haemoptysis, Week 36 (n=60, 16)	-1.67 (± 17.81)	-6.25 (± 18.13)		
Haemoptysis, Week 42 (n=53, 14)	-1.26 (± 15.96)	-2.38 (± 20.52)		

Haemoptysis, Week 48 (n=44, 12)	-3.79 (± 12.89)	-5.56 (± 19.25)		
Haemoptysis, Week 57 (n=36, 8)	-2.78 (± 18.47)	-8.33 (± 23.57)		
Haemoptysis, Week 66 (n=31, 5)	-2.15 (± 11.97)	0.00 (± 0.00)		
Haemoptysis, Week 75 (n=25, 4)	-1.33 (± 11.71)	0.00 (± 0.00)		
Haemoptysis, Week 84 (n=19, 3)	-3.51 (± 10.51)	0.00 (± 0.00)		
Haemoptysis, Week 93 (n=20, 2)	-1.67 (± 13.13)	0.00 (± 0.00)		
Haemoptysis, Week 102 (n=16, 1)	-2.08 (± 8.33)	0.00 (± 99999)		
Haemoptysis, Week 111 (n=14, 0)	-2.38 (± 8.91)	00000 (± 00000)		
Haemoptysis, Week 120 (n=14, 0)	-2.38 (± 8.91)	00000 (± 00000)		
Haemoptysis, Week 129 (n=14, 0)	-2.38 (± 8.91)	00000 (± 00000)		
Haemoptysis, Week 138 (n=14, 0)	-2.38 (± 8.91)	00000 (± 00000)		
Haemoptysis, Week 147 (n=14, 0)	-2.38 (± 8.91)	00000 (± 00000)		
Haemoptysis, Week 156 (n=7, 0)	0.00 (± 0.00)	00000 (± 00000)		
Haemoptysis, Week 165 (n=8, 0)	0.00 (± 0.00)	00000 (± 00000)		
Haemoptysis, Week 174 (n=7, 0)	0.00 (± 0.00)	00000 (± 00000)		
Haemoptysis, Week 183 (n=4, 0)	0.00 (± 0.00)	00000 (± 00000)		
Haemoptysis, Week 192 (n=2, 0)	0.00 (± 0.00)	00000 (± 00000)		
Haemoptysis, Week 201 (n=14, 0)	0.00 (± 0.00)	00000 (± 00000)		
Haemoptysis, Week 210 (n=1, 0)	0.00 (± 99999)	00000 (± 00000)		
Haemoptysis, Safety Follow-Up Visit (n=11, 13)	3.03 (± 17.98)	-2.56 (± 16.45)		
Sore Mouth, Baseline (n=296, 146)	4.17 (± 13.50)	5.02 (± 14.83)		
Sore Mouth, Week 6 (n=223, 115)	1.64 (± 19.30)	0.00 (± 20.23)		
Sore Mouth, Week 12 (n=150, 64)	-0.22 (± 17.91)	0.00 (± 16.80)		
Sore Mouth, Week 18 (n=122, 39)	-0.82 (± 16.85)	2.56 (± 20.78)		
Sore Mouth, Week 24 (n=105, 29)	-1.90 (± 19.52)	2.30 (± 17.66)		
Sore Mouth, Week 30 (n=84, 23)	-3.57 (± 21.96)	0.00 (± 17.41)		
Sore Mouth, Week 36 (n=61, 16)	-2.73 (± 22.19)	-2.08 (± 19.12)		
Sore Mouth, Week 42 (n=53, 14)	0.00 (± 29.24)	4.76 (± 28.81)		
Sore Mouth, Week 48 (n=44, 12)	-5.30 (± 18.94)	-2.78 (± 22.29)		
Sore Mouth, Week 57 (n=36, 8)	-5.56 (± 20.31)	0.00 (± 17.82)		
Sore Mouth, Week 66 (n=32, 5)	-4.17 (± 16.40)	6.67 (± 14.91)		
Sore Mouth, Week 75 (n=25, 4)	-5.33 (± 15.75)	16.67 (± 19.25)		

Sore Mouth, Week 84 (n=19, 3)	-1.75 (± 7.65)	11.11 (± 19.25)		
Sore Mouth, Week 93 (n=20, 2)	-1.67 (± 7.45)	0.00 (± 0.00)		
Sore Mouth, Week 102 (n=16, 1)	2.08 (± 8.33)	0.00 (± 99999)		
Sore Mouth, Week 111 (n=14, 0)	0.00 (± 22.65)	00000 (± 00000)		
Sore Mouth, Week 120 (n=14, 0)	2.38 (± 8.91)	00000 (± 00000)		
Sore Mouth, Week 129 (n=14, 0)	-4.76 (± 17.82)	00000 (± 00000)		
Sore Mouth, Week 138 (n=14, 0)	2.38 (± 8.91)	00000 (± 00000)		
Sore Mouth, Week 147 (n=14, 0)	0.00 (± 0.00)	00000 (± 00000)		
Sore Mouth, Week 156 (n=7, 0)	0.00 (± 0.00)	00000 (± 00000)		
Sore Mouth, Week 165 (n=8, 0)	4.17 (± 27.82)	00000 (± 00000)		
Sore Mouth, Week 174 (n=7, 0)	0.00 (± 0.00)	00000 (± 00000)		
Sore Mouth, Week 183 (n=4, 0)	0.00 (± 0.00)	00000 (± 00000)		
Sore Mouth, Week 192 (n=4, 0)	0.00 (± 0.00)	00000 (± 00000)		
Sore Mouth, Week 201 (n=2, 0)	0.00 (± 0.00)	00000 (± 00000)		
Sore Mouth, Week 210 (n=1, 0)	0.00 (± 99999)	00000 (± 00000)		
Sore Mouth, Safety Follow-Up Visit (n=11, 13)	27.27 (± 32.72)	0.00 (± 19.25)		
Dysphagia, Baseline (n=296, 146)	11.15 (± 23.60)	8.68 (± 19.60)		
Dysphagia, Week 6 (n=223, 115)	-1.20 (± 20.47)	2.90 (± 25.96)		
Dysphagia, Week 12 (n=151, 64)	-0.44 (± 21.77)	-1.04 (± 23.73)		
Dysphagia, Week 18 (n=122, 39)	-2.19 (± 23.37)	-0.85 (± 29.11)		
Dysphagia, Week 24 (n=106, 30)	-4.72 (± 23.20)	1.11 (± 28.34)		
Dysphagia, Week 30 (n=84, 23)	-3.57 (± 23.15)	2.90 (± 28.27)		
Dysphagia, Week 36 (n=60, 16)	-6.11 (± 28.45)	6.25 (± 13.44)		
Dysphagia, Week 42 (n=53, 14)	-7.55 (± 31.11)	4.76 (± 17.82)		
Dysphagia, Week 48 (n=44, 12)	-5.30 (± 23.78)	0.00 (± 14.21)		
Dysphagia, Week 57 (n=36, 8)	-3.70 (± 29.58)	4.17 (± 21.36)		
Dysphagia, Week 66 (n=31, 5)	-6.45 (± 32.68)	0.00 (± 0.00)		
Dysphagia, Week 75 (n=25, 4)	-4.00 (± 27.76)	16.67 (± 33.33)		
Dysphagia, Week 84 (n=19, 3)	-8.77 (± 33.04)	0.00 (± 0.00)		
Dysphagia, Week 93 (n=20, 2)	0.00 (± 28.61)	0.00 (± 0.00)		
Dysphagia, Week 102 (n=16, 1)	0.00 (± 0.00)	0.00 (± 99999)		
Dysphagia, Week 111 (n=14, 0)	-4.76 (± 22.10)	00000 (± 00000)		

Dysphagia, Week 120 (n=14, 0)	2.38 (± 8.91)	00000 (± 00000)		
Dysphagia, Week 129 (n=14, 0)	-2.38 (± 20.52)	00000 (± 00000)		
Dysphagia, Week 138 (n=14, 0)	4.76 (± 12.10)	00000 (± 00000)		
Dysphagia, Week 147 (n=14, 0)	-4.76 (± 28.81)	00000 (± 00000)		
Dysphagia, Week 156 (n=7, 0)	0.00 (± 0.00)	00000 (± 00000)		
Dysphagia, Week 165 (n=8, 0)	-8.33 (± 23.57)	00000 (± 00000)		
Dysphagia, Week 174 (n=7, 0)	0.00 (± 0.00)	00000 (± 00000)		
Dysphagia, Week 183 (n=4, 0)	0.00 (± 0.00)	00000 (± 00000)		
Dysphagia, Week 192 (n=4, 0)	0.00 (± 0.00)	00000 (± 00000)		
Dysphagia, Week 201 (n=2, 0)	16.67 (± 23.57)	00000 (± 00000)		
Dysphagia, Week 210 (n=1, 0)	0.00 (± 99999)	00000 (± 00000)		
Dysphagia, Safety Follow-Up Visit (n=11, 13)	12.12 (± 37.34)	0.00 (± 19.25)		
Peripheral Neuropathy, Baseline (n=296, 146)	11.26 (± 21.10)	14.84 (± 24.46)		
Peripheral Neuropathy, Week 6 (n=223, 115)	3.29 (± 19.74)	1.45 (± 25.51)		
Peripheral Neuropathy, Week 12 (n=151, 64)	1.99 (± 21.16)	2.08 (± 26.48)		
Peripheral Neuropathy, Week 18 (n=121, 39)	1.10 (± 19.21)	5.13 (± 24.83)		
Peripheral Neuropathy, Week 24 (n=106, 30)	3.77 (± 23.60)	7.78 (± 22.63)		
Peripheral Neuropathy, Week 30 (n=83, 23)	4.82 (± 20.25)	-1.45 (± 21.27)		
Peripheral Neuropathy, Week 36 (n=60, 16)	7.78 (± 24.83)	12.50 (± 29.50)		
Peripheral Neuropathy, Week 42 (n=53, 14)	8.18 (± 23.48)	9.52 (± 20.37)		
Peripheral Neuropathy, Week 48 (n=44, 12)	6.82 (± 23.38)	8.33 (± 20.72)		
Peripheral Neuropathy, Week 57 (n=36, 8)	7.41 (± 25.34)	20.83 (± 30.54)		
Peripheral Neuropathy, Week 66 (n=32, 5)	6.25 (± 23.09)	13.33 (± 38.01)		
Peripheral Neuropathy, Week 75 (n=25, 4)	5.33 (± 22.93)	8.33 (± 31.91)		
Peripheral Neuropathy, Week 84 (n=19, 3)	8.77 (± 21.78)	0.00 (± 0.00)		
Peripheral Neuropathy, Week 93 (n=20, 2)	6.67 (± 17.44)	0.00 (± 0.00)		
Peripheral Neuropathy, Week 102 (n=16, 1)	6.25 (± 18.13)	0.00 (± 99999)		
Peripheral Neuropathy, Week 111 (n=14, 0)	2.38 (± 15.82)	00000 (± 00000)		
Peripheral Neuropathy, Week 120 (n=14, 0)	2.38 (± 15.82)	00000 (± 00000)		
Peripheral Neuropathy, Week 129 (n=14, 0)	2.38 (± 15.82)	00000 (± 00000)		
Peripheral Neuropathy, Week 138 (n=14, 0)	0.00 (± 13.07)	00000 (± 00000)		

Peripheral Neuropathy, Week 147 (n=14, 0)	2.38 (± 15.82)	00000 (± 00000)		
Peripheral Neuropathy, Week 156 (n=7, 0)	-4.76 (± 12.60)	00000 (± 00000)		
Peripheral Neuropathy, Week 165 (n=8, 0)	0.00 (± 17.82)	00000 (± 00000)		
Peripheral Neuropathy, Week 174 (n=7, 0)	-4.76 (± 12.60)	00000 (± 00000)		
Peripheral Neuropathy, Week 183 (n=4, 0)	-8.33 (± 16.67)	00000 (± 00000)		
Peripheral Neuropathy, Week 192 (n=4, 0)	16.67 (± 43.03)	00000 (± 00000)		
Peripheral Neuropathy, Week 201 (n=2, 0)	0.00 (± 0.00)	00000 (± 00000)		
Peripheral Neuropathy, Week 210 (n=1, 0)	0.00 (± 99999)	00000 (± 00000)		
Peripheral Neuropathy, SFUV (n=11, 12)	21.21 (± 40.20)	-2.78 (± 33.21)		
Alopecia, Baseline (n=295, 145)	7.91 (± 20.70)	4.83 (± 15.70)		
Alopecia, Week 6 (n=220, 115)	-1.06 (± 19.48)	6.09 (± 27.07)		
Alopecia, Week 12 (n=149, 63)	-2.01 (± 17.43)	7.94 (± 27.90)		
Alopecia, Week 18 (n=121, 39)	-1.93 (± 17.90)	12.82 (± 23.71)		
Alopecia, Week 24 (n=105, 28)	-1.27 (± 17.86)	14.29 (± 30.67)		
Alopecia, Week 30 (n=83, 23)	-1.20 (± 19.79)	10.14 (± 27.40)		
Alopecia, Week 36 (n=60, 16)	5.56 (± 17.54)	10.42 (± 29.11)		
Alopecia, Week 42 (n=52, 14)	3.85 (± 14.24)	7.14 (± 29.75)		
Alopecia, Week 48 (n=43, 12)	3.10 (± 17.54)	13.89 (± 36.12)		
Alopecia, Week 57 (n=35, 8)	7.62 (± 18.23)	29.17 (± 27.82)		
Alopecia, Week 66 (n=30, 5)	6.67 (± 13.56)	6.67 (± 14.91)		
Alopecia, Week 75 (n=24, 4)	5.56 (± 12.69)	8.33 (± 16.67)		
Alopecia, Week 84 (n=19, 3)	1.75 (± 7.65)	11.11 (± 19.25)		
Alopecia, Week 93 (n=20, 2)	5.00 (± 12.21)	16.67 (± 23.57)		
Alopecia, Week 102 (n=16, 1)	4.17 (± 11.39)	33.33 (± 99999)		
Alopecia, Week 111 (n=14, 0)	2.38 (± 8.91)	00000 (± 00000)		
Alopecia, Week 120 (n=14, 0)	4.76 (± 12.10)	00000 (± 00000)		
Alopecia, Week 129 (n=14, 0)	2.38 (± 8.91)	00000 (± 00000)		
Alopecia, Week 138 (n=14, 0)	7.14 (± 19.30)	00000 (± 00000)		
Alopecia, Week 147 (n=14, 0)	2.38 (± 8.91)	00000 (± 00000)		
Alopecia, Week 156 (n=7, 0)	0.00 (± 0.00)	00000 (± 00000)		
Alopecia, Week 165 (n=8, 0)	0.00 (± 0.00)	00000 (± 00000)		
Alopecia, Week 174 (n=7, 0)	0.00 (± 0.00)	00000 (± 00000)		

Alopecia, Week 183 (n=4, 0)	0.00 (± 0.00)	00000 (± 00000)		
Alopecia, Week 192 (n=4, 0)	8.33 (± 16.67)	00000 (± 00000)		
Alopecia, Week 201 (n=2, 0)	16.67 (± 23.57)	00000 (± 00000)		
Alopecia, Week 210 (n=1, 0)	0.00 (± 99999)	00000 (± 00000)		
Alopecia, SFUV (n=11, 13)	0.00 (± 0.00)	12.82 (± 44.18)		
Pain in Chest, Baseline (n=294, 144)	20.29 (± 26.70)	19.91 (± 24.72)		
Pain in Chest, Week 6 (n=218, 114)	-2.45 (± 26.66)	-4.09 (± 29.79)		
Pain in Chest, Week 12 (n=149, 63)	-4.03 (± 27.65)	-5.29 (± 31.80)		
Pain in Chest, Week 18 (n=121, 38)	-9.37 (± 27.29)	-5.26 (± 26.31)		
Pain in Chest, Week 24 (n=105, 29)	-7.62 (± 28.22)	-2.30 (± 28.07)		
Pain in Chest, Week 30 (n=83, 22)	-7.23 (± 31.26)	-9.09 (± 34.40)		
Pain in Chest, Week 36 (n=60, 14)	-11.67 (± 29.96)	2.38 (± 30.56)		
Pain in Chest, Week 42 (n=52, 13)	-11.54 (± 34.86)	-2.56 (± 31.80)		
Pain in Chest, Week 48 (n=43, 11)	-17.83 (± 28.50)	3.03 (± 17.98)		
Pain in Chest, Week 57 (n=35, 7)	-18.10 (± 30.62)	-4.76 (± 23.00)		
Pain in Chest, Week 66 (n=31, 4)	-15.05 (± 34.25)	-16.67 (± 19.25)		
Pain in Chest, Week 75 (n=24, 3)	-13.89 (± 21.80)	-22.22 (± 19.25)		
Pain in Chest, Week 84 (n=19, 2)	-22.81 (± 31.53)	-16.67 (± 23.57)		
Pain in Chest, Week 93 (n=20, 1)	-23.33 (± 26.71)	0.00 (± 99999)		
Pain in Chest, Week 102 (n=16, 0)	-20.83 (± 31.91)	00000 (± 00000)		
Pain in Chest, Week 111 (n=14, 0)	-26.19 (± 29.75)	00000 (± 00000)		
Pain in Chest, Week 120 (n=14, 0)	-26.19 (± 29.75)	00000 (± 00000)		
Pain in Chest, Week 129 (n=14, 0)	-21.43 (± 21.11)	00000 (± 00000)		
Pain in Chest, Week 138 (n=14, 0)	-26.19 (± 29.75)	00000 (± 00000)		
Pain in Chest, Week 147 (n=14, 0)	-19.05 (± 36.31)	00000 (± 00000)		
Pain in Chest, Week 156 (n=7, 0)	-23.81 (± 25.20)	00000 (± 00000)		
Pain in Chest, Week 165 (n=8, 0)	-25.00 (± 23.57)	00000 (± 00000)		
Pain in Chest, Week 174 (n=7, 0)	-23.81 (± 25.20)	00000 (± 00000)		
Pain in Chest, Week 183 (n=4, 0)	-16.67 (± 33.33)	00000 (± 00000)		
Pain in Chest, Week 192 (n=4, 0)	-16.67 (± 33.33)	00000 (± 00000)		
Pain in Chest, Week 201 (n=2, 0)	-33.33 (± 47.14)	00000 (± 00000)		

Pain in Chest, Week 210 (n=1, 0)	-66.67 (± 99999)	00000 (± 00000)		
Pain in Chest, SFUV (n=11, 13)	0.00 (± 21.08)	12.82 (± 21.68)		
Pain in Arm or Shoulder, Baseline (n=294, 145)	19.16 (± 28.08)	19.08 (± 27.43)		
Pain in Arm or Shoulder, Week 6 (n=221, 114)	-0.45 (± 26.87)	-0.58 (± 29.07)		
Pain in Arm or Shoulder, Week 12 (n=149, 63)	0.67 (± 29.38)	-4.23 (± 30.81)		
Pain in Arm or Shoulder, Week 18 (n=121, 38)	-1.65 (± 30.08)	-2.63 (± 34.99)		
Pain in Arm or Shoulder, Week 24 (n=104, 28)	-3.21 (± 27.68)	0.00 (± 28.69)		
Pain in Arm or Shoulder, Week 30 (n=83, 22)	-0.40 (± 26.80)	4.55 (± 25.81)		
Pain in Arm or Shoulder, Week 36 (n=60, 15)	-4.44 (± 23.34)	-2.22 (± 34.43)		
Pain in Arm or Shoulder, Week 42 (n=53, 13)	-1.89 (± 25.67)	-5.13 (± 38.12)		
Pain in Arm or Shoulder, Week 48 (n=44, 11)	-1.52 (± 28.71)	-6.06 (± 35.96)		
Pain in Arm or Shoulder, Week 57 (n=36, 7)	7.41 (± 25.34)	-9.52 (± 37.09)		
Pain in Arm or Shoulder, Week 66 (n=31, 4)	1.08 (± 26.50)	-33.33 (± 38.49)		
Pain in Arm or Shoulder, Week 75 (n=24, 3)	-1.39 (± 26.88)	-33.33 (± 33.33)		
Pain in Arm or Shoulder, Week 84 (n=19, 2)	3.51 (± 24.58)	-16.67 (± 23.57)		
Pain in Arm or Shoulder, Week 93 (n=20, 1)	6.67 (± 23.20)	0.00 (± 99999)		
Pain in Arm or Shoulder, Week 102 (n=16, 0)	8.33 (± 25.82)	00000 (± 00000)		
Pain in Arm or Shoulder, Week 111 (n=14, 0)	2.38 (± 27.62)	00000 (± 00000)		
Pain in Arm or Shoulder, Week 120 (n=14, 0)	4.76 (± 25.68)	00000 (± 00000)		
Pain in Arm or Shoulder, Week 129 (n=14, 0)	2.38 (± 27.62)	00000 (± 00000)		
Pain in Arm or Shoulder, Week 138 (n=14, 0)	2.38 (± 24.33)	00000 (± 00000)		
Pain in Arm or Shoulder, Week 147 (n=14, 0)	2.38 (± 27.62)	00000 (± 00000)		
Pain in Arm or Shoulder, Week 156 (n=7, 0)	9.52 (± 16.27)	00000 (± 00000)		
Pain in Arm or Shoulder, Week 165 (n=8, 0)	4.17 (± 11.79)	00000 (± 00000)		
Pain in Arm or Shoulder, Week 174 (n=7, 0)	0.00 (± 0.00)	00000 (± 00000)		
Pain in Arm or Shoulder, Week 183 (n=4, 0)	25.00 (± 31.91)	00000 (± 00000)		
Pain in Arm or Shoulder, Week 192 (n=4, 0)	0.00 (± 0.00)	00000 (± 00000)		
Pain in Arm or Shoulder, Week 201 (n=2, 0)	0.00 (± 0.00)	00000 (± 00000)		
Pain in Arm or Shoulder, Week 210 (n=1, 0)	0.00 (± 99999)	00000 (± 00000)		
Pain in Arm or Shoulder, SFUV (n=11, 13)	12.12 (± 42.88)	7.69 (± 33.76)		
Pain in other parts, Baseline (n=287, 144)	25.32 (± 31.93)	27.55 (± 31.86)		

Pain in other parts, Week 6 (n=216, 113)	-1.85 (± 29.05)	1.18 (± 33.31)		
Pain in other parts, Week 12 (n=147, 62)	-0.91 (± 32.63)	-0.54 (± 34.93)		
Pain in other parts, Week 18 (n=115, 36)	-1.74 (± 36.63)	11.11 (± 36.51)		
Pain in other parts, Week 24 (n=104, 28)	-3.53 (± 35.35)	-4.76 (± 38.18)		
Pain in other parts, Week 30 (n=81, 22)	-2.88 (± 38.08)	-7.58 (± 20.40)		
Pain in other parts, Week 36 (n=59, 15)	-5.08 (± 33.23)	2.22 (± 29.46)		
Pain in other parts, Week 42 (n=50, 13)	-2.67 (± 33.56)	-12.82 (± 32.03)		
Pain in other parts, Week 48 (n=43, 11)	-4.65 (± 27.78)	-15.15 (± 34.52)		
Pain in other parts, Week 57 (n=34, 7)	-1.96 (± 34.76)	-9.52 (± 31.71)		
Pain in other parts, Week 66 (n=29, 4)	3.45 (± 37.10)	-16.67 (± 43.03)		
Pain in other parts, Week 75 (n=24, 3)	8.33 (± 31.47)	0.00 (± 0.00)		
Pain in other parts, Week 84 (n=19, 2)	-1.75 (± 39.24)	0.00 (± 0.00)		
Pain in other parts, Week 93 (n=20, 1)	-3.33 (± 28.41)	0.00 (± 99999)		
Pain in other parts, Week 102 (n=16, 0)	-4.17 (± 26.87)	00000 (± 00000)		
Pain in other parts, Week 111 (n=13, 0)	-5.13 (± 29.96)	00000 (± 00000)		
Pain in other parts, Week 120 (n=14, 0)	0.00 (± 26.15)	00000 (± 00000)		
Pain in other parts, Week 129 (n=14, 0)	-7.14 (± 14.19)	00000 (± 00000)		
Pain in other parts, Week 138 (n=14, 0)	-7.14 (± 19.30)	00000 (± 00000)		
Pain in other parts, Week 147 (n=14, 0)	0.00 (± 18.49)	00000 (± 00000)		
Pain in other parts, Week 156 (n=7, 0)	-14.29 (± 26.23)	00000 (± 00000)		
Pain in other parts, Week 165 (n=8, 0)	-16.67 (± 25.20)	00000 (± 00000)		
Pain in other parts, Week 174 (n=7, 0)	-9.52 (± 31.71)	00000 (± 00000)		
Pain in other parts, Week 183 (n=4, 0)	8.33 (± 63.10)	00000 (± 00000)		
Pain in other parts, Week 192 (n=4, 0)	-8.33 (± 31.91)	00000 (± 00000)		
Pain in other parts, Week 201 (n=2, 0)	-33.33 (± 0.00)	00000 (± 00000)		
Pain in other parts, Week 210 (n=1, 0)	-66.67 (± 99999)	00000 (± 00000)		
Pain in other parts, SFUV (n=11, 13)	9.09 (± 42.40)	0.00 (± 33.33)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Deterioration (TTD) in Patient-Reported Lung Cancer Symptoms as Assessed by EORTC QLQ-C30 Score

End point title	Time to Deterioration (TTD) in Patient-Reported Lung Cancer Symptoms as Assessed by EORTC QLQ-C30 Score

End point description:

TTD with use of the EORTC was defined as the time from randomization to the first confirmed clinically meaningful deterioration in EORTC symptom scores. Confirmed clinically meaningful deterioration in lung cancer symptoms was defined as a =10-point increase above baseline in a symptom score that must be held for at least two consecutive assessments or an initial = 10-point increase above baseline followed by either (a) death within 6 weeks from the last assessment through Week 48 or (b) death within 9 weeks from the last assessment from Week 48 thereafter. A = 10-point change in the EORTC scale score was perceived by participants as clinically significant (Osoba et al. 1998). '88888"=not estimable. ITT population included all randomized participants irrespective of whether the assigned treatment was actually received.

End point type	Secondary

End point timeframe:

From baseline up to approximately 55 months

End point values	Atezolizumab	Single Agent Chemotherapy (Vinorelbine or Gemcitabine)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	302	151		
Units: Months				
median (confidence interval 95%)				
Dyspnoea	88888 (19.0 to 88888)	88888 (8.3 to 88888)		
Fatigue	13.5 (8.3 to 88888)	8.4 (5.6 to 88888)		

Statistical analyses

Statistical analysis title	Statistical Analysis

Statistical analysis description:

Time to deterioration for Fatigue (multi items QLQ-C30)

Comparison groups	Atezolizumab v Single Agent Chemotherapy (Vinorelbine or Gemcitabine)
Number of subjects included in analysis	453
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.62
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.55
upper limit	1.42

Notes:

[1] - Stratified analysis. Histologic subtype, PD-L1 IHC status and brain metastases (Yes/No) were added as stratification factors.

Statistical analysis title	Statistical Analysis
Statistical analysis description:	
Time to deterioration for Dyspnoea (single item QLQ-C30)	
Comparison groups	Atezolizumab v Single Agent Chemotherapy (Vinorelbine or Gemcitabine)
Number of subjects included in analysis	453
Analysis specification	Pre-specified
Analysis type	superiority[2]
P-value	= 0.975
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.57
upper limit	1.78

Notes:

[2] - Stratified analysis. Histologic subtype, PD-L1 IHC status and brain metastases (Yes/No) were added as stratification factors.

Secondary: TTD in Patient-Reported Lung Cancer Symptoms As Assessed by EORTC QLQ-LC13 Score

End point title	TTD in Patient-Reported Lung Cancer Symptoms As Assessed by EORTC QLQ-LC13 Score

End point description:

TTD with use of the EORTC = time from randomization to the first confirmed clinically meaningful deterioration in EORTC symptom scores. Confirmed clinically meaningful deterioration in lung cancer symptoms was = 10-point increase above baseline in a symptom score that must be held for at least two consecutive assessments/an initial = 10-point increase above baseline followed by either (a) death within 6 weeks from the last assessment through Week 48 or (b) death within 9 weeks from the last assessment from Week 48 thereafter. A = 10-point change in the EORTC scale score was perceived by participants as clinically significant. '88888"=not estimable. ITT population included all randomized participants irrespective of whether the assigned treatment was actually received.

End point type	Secondary

End point timeframe:

From baseline up to approximately 55 months

End point values	Atezolizumab	Single Agent Chemotherapy (Vinorelbine or Gemcitabine)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	302	151		
Units: Months				
median (confidence interval 95%)				
Cough	88888 (88888 to 88888)	21.4 (13.9 to 88888)		
Chest Pain	88888 (88888 to 88888)	88888 (6.8 to 88888)		

Dyspnoea	17.3 (9.6 to 34.2)	8.3 (5.5 to 88888)		
Arm and/or Shoulder Pain	21.3 (13.6 to 88888)	13.9 (8.6 to 88888)		
Composite of Cough, Dyspnea and Chest Pain	8.3 (5.5 to 17.3)	4.2 (2.9 to 5.6)		

Statistical analyses

Statistical analysis title	Statistical Analysis
Statistical analysis description:	
Time to deterioration for Cough (single item QLQ-LC13)	
Comparison groups	Atezolizumab v Single Agent Chemotherapy (Vinorelbine or Gemcitabine)
Number of subjects included in analysis	453
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	= 0.653
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	2.26

Notes:

[3] - Stratified analysis. Histologic subtype, PD-L1 IHC status and brain metastases (Yes/No) were added as stratification factors.

Statistical analysis title	Statistical Analysis
Statistical analysis description:	
Time to deterioration for Chest pain (single item QLQ-LC13)	
Comparison groups	Atezolizumab v Single Agent Chemotherapy (Vinorelbine or Gemcitabine)
Number of subjects included in analysis	453
Analysis specification	Pre-specified
Analysis type	superiority[4]
P-value	= 0.036
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.27
upper limit	0.97

Notes:

[4] - Stratified analysis. Histologic subtype, PD-L1 IHC status and brain metastases (Yes/No) were added as stratification factors.

Statistical analysis title	Statistical Analysis

Statistical analysis description:	
Time to deterioration for Dyspnoea (multiple items QLQ-LC13)	
Comparison groups	Atezolizumab v Single Agent Chemotherapy (Vinorelbine or Gemcitabine)
Number of subjects included in analysis	453
Analysis specification	Pre-specified
Analysis type	superiority[5]
P-value	= 0.125
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.45
upper limit	1.11

Notes:

[5] - Stratified analysis. Histologic subtype, PD-L1 IHC status and brain metastases (Yes/No) were added as stratification factors.

Statistical analysis title	Statistical Analysis
Statistical analysis description:	
Time to deterioration for Arm and/or shoulder pain (single item QLQ-LC13)	
Comparison groups	Atezolizumab v Single Agent Chemotherapy (Vinorelbine or Gemcitabine)
Number of subjects included in analysis	453
Analysis specification	Pre-specified
Analysis type	superiority[6]
P-value	= 0.362
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.41
upper limit	1.39

Notes:

[6] - Stratified analysis. Histologic subtype, PD-L1 IHC status and brain metastases (Yes/No) were added as stratification factors.

Statistical analysis title	Statistical Analysis
Statistical analysis description:	
Time to Confirmed Deterioration for the Composite of the 3 following symptoms: cough, dyspnoea (multi-items QLQ-LC13) and chest pain	
Comparison groups	Atezolizumab v Single Agent Chemotherapy (Vinorelbine or Gemcitabine)
Number of subjects included in analysis	453
Analysis specification	Pre-specified
Analysis type	superiority[7]
P-value	= 0.041
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.68

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.46
upper limit	0.99

Notes:

[7] - Stratified analysis. Histologic subtype, PD-L1 IHC status and brain metastases (Yes/No) were added as stratification factors.

Secondary: PFS, as Determined by the Investigator Using RECIST v1.1 in Participants With PD-L1 Positive Status

End point title	PFS, as Determined by the Investigator Using RECIST v1.1 in Participants With PD-L1 Positive Status

End point description:

PFS was defined as the time from randomization to the first documented disease progression as determined by the investigator with the use of RECIST v1.1 or death from any cause, whichever occurs first. PD was defined as at least 20% increase in the sum of diameters of lesions, taking as reference the smallest sum during the study (nadir), including baseline. Investigator-assessed PFS was assessed in participants whose tumors express PD-L1 protein as measured by PD-L1 SP263 IHC assay. KM estimates were used to calculate the median. ITT Population included all randomized participants irrespective of whether the assigned treatment was actually received. Number analyzed is the number of participants with data available for analysis.

End point type	Secondary

End point timeframe:

From randomization to the first occurence of disease progression or death from any cause, whichever occurs first (up to approximately 55 months)

End point values	Atezolizumab	Single Agent Chemotherapy (Vinorelbine or Gemcitabine)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	127	78		
Units: Months				
median (confidence interval 95%)				
SP263 TC>=1%	4.2 (2.9 to 5.8)	3.0 (2.8 to 5.4)		

Statistical analyses

Statistical analysis title	PFS SP263 TC>=1%

Statistical analysis description:

SP263 TC>=1%

Comparison groups	Atezolizumab v Single Agent Chemotherapy (Vinorelbine or Gemcitabine)
Number of subjects included in analysis	205
Analysis specification	Pre-specified
Analysis type	superiority[8]
P-value	= 0.366
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.87

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.64
upper limit	1.18

Notes:

[8] - Stratified analysis. Histologic subtype, PD-L1 IHC status and brain metastases (Yes/No) were added as stratification factors.

Secondary: OS in Participants With Programmed Death-Ligand 1 (PD-L1) Positive Status

End point title	OS in Participants With Programmed Death-Ligand 1 (PD-L1) Positive Status

End point description:

OS was defined as the time between the date of randomization and the date of death due to any cause. OS was assessed in participants whose tumors express PD-L1 protein (i.e., tumor cell (TC) ≥1%) as measured by PD-L1 SP263 immunohistochemistry (IHC) assay. KM estimates were used to calculate the median. ITT Population included all randomized participants irrespective of whether the assigned treatment was actually received. Number analyzed is the number of participants with data available for analysis.

End point type	Secondary

End point timeframe:

From randomization up to death from any cause (up to approximately 55 months)

End point values	Atezolizumab	Single Agent Chemotherapy (Vinorelbine or Gemcitabine)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	127	78		
Units: Months				
median (confidence interval 95%)				
SP263 TC>=1%	9.4 (7.0 to 11.3)	10.3 (7.1 to 12.3)		

Statistical analyses

Statistical analysis title	OS SP263 TC>=1% Statistical Analysis

Statistical analysis description:

SP263 TC>=1%

Comparison groups	Atezolizumab v Single Agent Chemotherapy (Vinorelbine or Gemcitabine)
Number of subjects included in analysis	205
Analysis specification	Pre-specified
Analysis type	superiority[9]
P-value	= 0.272
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.84

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.61
upper limit	1.15

Notes:

[9] - Stratified analysis. Histologic subtype, PD-L1 IHC status and brain metastases (Yes/No) were added as stratification factors.

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From Day 1 up to 90 days after last atezolizumab dose (up to approximately 62 months)	
Adverse event reporting additional description:	
Safety population included participants who received any amount of any study drug.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups	
Reporting group title	Single Agent Chemotherapy (Vinorelbine or Gemcitabine)
Reporting group description:	
Participants received single agent chemotherapy; either vinorelbine oral or IV, or gemcitabine IV, according to the label based on investigator's choice until disease progression unacceptable toxicity, participant or physician decision to discontinue, or death.	
Reporting group title	Atezolizumab
Reporting group description:	
Participants received atezolizumab 1200 mg, as IV infusion on Day 1 of each 21-day cycle until loss of clinical benefit, unacceptable toxicity, participant or physician decision to discontinue, or death.	

Serious adverse events	Single Agent Chemotherapy (Vinorelbine or Gemcitabine)	Atezolizumab	
Total subjects affected by serious adverse events			
subjects affected / exposed	54 / 147 (36.73%)	147 / 300 (49.00%)	
number of deaths (all causes)	129	248	
number of deaths resulting from adverse events	13	35	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Iliac artery dissection			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Superior vena cava occlusion			

subjects affected / exposed	1 / 147 (0.68%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral ischaemia			
subjects affected / exposed	1 / 147 (0.68%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	0 / 147 (0.00%)	2 / 300 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Capillary leak syndrome			
subjects affected / exposed	1 / 147 (0.68%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Infusion site extravasation			
subjects affected / exposed	1 / 147 (0.68%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalised oedema			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	1 / 147 (0.68%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Death			
subjects affected / exposed	2 / 147 (1.36%)	7 / 300 (2.33%)	
occurrences causally related to treatment / all	0 / 2	0 / 7	
deaths causally related to treatment / all	0 / 2	0 / 7	
Chest pain			

subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthenia			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema			
subjects affected / exposed	1 / 147 (0.68%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Performance status decreased			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 147 (0.68%)	3 / 300 (1.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden cardiac death			
subjects affected / exposed	0 / 147 (0.00%)	2 / 300 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Non-cardiac chest pain			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Systemic immune activation			

subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Hypoxia			
subjects affected / exposed	1 / 147 (0.68%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Haemoptysis			
subjects affected / exposed	2 / 147 (1.36%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	1 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	2 / 147 (1.36%)	6 / 300 (2.00%)	
occurrences causally related to treatment / all	0 / 2	1 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	2 / 147 (1.36%)	7 / 300 (2.33%)	
occurrences causally related to treatment / all	0 / 2	1 / 7	
deaths causally related to treatment / all	0 / 0	0 / 1	
Asthma			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory failure			

subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune-mediated lung disease			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal haemorrhage			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	2 / 147 (1.36%)	9 / 300 (3.00%)	
occurrences causally related to treatment / all	0 / 2	1 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	2 / 147 (1.36%)	8 / 300 (2.67%)	
occurrences causally related to treatment / all	1 / 2	8 / 9	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumothorax			
subjects affected / exposed	0 / 147 (0.00%)	3 / 300 (1.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pulmonary embolism			
subjects affected / exposed	3 / 147 (2.04%)	3 / 300 (1.00%)	
occurrences causally related to treatment / all	0 / 3	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary hypertension			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory arrest			

subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Respiratory failure			
subjects affected / exposed	1 / 147 (0.68%)	2 / 300 (0.67%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 147 (0.00%)	2 / 300 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disorientation			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Eastern Cooperative Oncology Group performance status worsened			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 147 (0.68%)	2 / 300 (0.67%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			
subjects affected / exposed	0 / 147 (0.00%)	2 / 300 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			

subjects affected / exposed	0 / 147 (0.00%)	2 / 300 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar vertebral fracture			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radiation oesophagitis			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac failure congestive			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	0 / 147 (0.00%)	2 / 300 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Acute left ventricular failure			

subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Acute coronary syndrome			
subjects affected / exposed	2 / 147 (1.36%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorder			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac failure			
subjects affected / exposed	0 / 147 (0.00%)	3 / 300 (1.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	1 / 147 (0.68%)	3 / 300 (1.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus tachycardia			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocarditis			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial ischaemia			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			

subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Ischaemic stroke			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral infarction			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	2 / 147 (1.36%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage intracranial			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic cerebral infarction			
subjects affected / exposed	1 / 147 (0.68%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	1 / 147 (0.68%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			

subjects affected / exposed	0 / 147 (0.00%)	2 / 300 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal cord compression			
subjects affected / exposed	1 / 147 (0.68%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myasthenia gravis			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Lacunar stroke			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lacunar infarction			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	1 / 147 (0.68%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelosuppression			
subjects affected / exposed	2 / 147 (1.36%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukocytosis			

subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	3 / 147 (2.04%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	3 / 3	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Disseminated intravascular coagulation			
subjects affected / exposed	1 / 147 (0.68%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia			
subjects affected / exposed	1 / 147 (0.68%)	2 / 300 (0.67%)	
occurrences causally related to treatment / all	1 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Small intestinal perforation			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal toxicity			

subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum intestinal			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	1 / 147 (0.68%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 147 (0.68%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	1 / 147 (0.68%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	1 / 147 (0.68%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis			

subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune-mediated hepatitis			
subjects affected / exposed	0 / 147 (0.00%)	2 / 300 (0.67%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	1 / 1	
Liver injury			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	1 / 147 (0.68%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute kidney injury			
subjects affected / exposed	2 / 147 (1.36%)	3 / 300 (1.00%)	
occurrences causally related to treatment / all	0 / 2	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Flank pain			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Fracture pain			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rheumatoid arthritis			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periarthritis			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	0 / 147 (0.00%)	5 / 300 (1.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 1	
Appendicitis			
subjects affected / exposed	1 / 147 (0.68%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain abscess			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	1 / 147 (0.68%)	2 / 300 (0.67%)	
occurrences causally related to treatment / all	1 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Infectious pleural effusion			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal infection			
subjects affected / exposed	1 / 147 (0.68%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	1 / 147 (0.68%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea infectious			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 147 (0.00%)	2 / 300 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Influenza			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	4 / 147 (2.72%)	5 / 300 (1.67%)	
occurrences causally related to treatment / all	0 / 5	0 / 5	
deaths causally related to treatment / all	0 / 2	0 / 1	
Neutropenic sepsis			

subjects affected / exposed	2 / 147 (1.36%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	11 / 147 (7.48%)	34 / 300 (11.33%)	
occurrences causally related to treatment / all	6 / 13	4 / 38	
deaths causally related to treatment / all	1 / 2	0 / 8	
Pneumonia aspiration			
subjects affected / exposed	0 / 147 (0.00%)	2 / 300 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumonia bacterial			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia fungal			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia pneumococcal			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Relapsing fever			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	1 / 147 (0.68%)	2 / 300 (0.67%)	
occurrences causally related to treatment / all	1 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			

subjects affected / exposed	4 / 147 (2.72%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	2 / 4	0 / 0	
deaths causally related to treatment / all	2 / 4	0 / 0	
Septic shock			
subjects affected / exposed	0 / 147 (0.00%)	2 / 300 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 2	
Skin infection			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 147 (0.00%)	3 / 300 (1.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Klebsiella urinary tract infection			
subjects affected / exposed	1 / 147 (0.68%)	0 / 300 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis salmonella			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoalbuminaemia			

subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	0 / 147 (0.00%)	3 / 300 (1.00%)	
occurrences causally related to treatment / all	0 / 0	6 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercalcaemia			
subjects affected / exposed	0 / 147 (0.00%)	2 / 300 (0.67%)	
occurrences causally related to treatment / all	0 / 0	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ketoacidosis			
subjects affected / exposed	0 / 147 (0.00%)	2 / 300 (0.67%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	0 / 147 (0.00%)	2 / 300 (0.67%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	0 / 147 (0.00%)	1 / 300 (0.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Single Agent Chemotherapy (Vinorelbine or Gemcitabine)	Atezolizumab	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	128 / 147 (87.07%)	234 / 300 (78.00%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	6 / 147 (4.08%)	23 / 300 (7.67%)	
occurrences (all)	8	39	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	19 / 147 (12.93%)	43 / 300 (14.33%)	
occurrences (all)	25	49	
Fatigue			
subjects affected / exposed	34 / 147 (23.13%)	58 / 300 (19.33%)	
occurrences (all)	34	74	
Oedema peripheral			
subjects affected / exposed	6 / 147 (4.08%)	25 / 300 (8.33%)	
occurrences (all)	6	28	
Pyrexia			
subjects affected / exposed	10 / 147 (6.80%)	30 / 300 (10.00%)	
occurrences (all)	18	35	
Respiratory, thoracic and mediastinal disorders			
Haemoptysis			
subjects affected / exposed	9 / 147 (6.12%)	19 / 300 (6.33%)	
occurrences (all)	10	26	
Dyspnoea			
subjects affected / exposed	14 / 147 (9.52%)	56 / 300 (18.67%)	
occurrences (all)	15	60	
Cough			
subjects affected / exposed	13 / 147 (8.84%)	59 / 300 (19.67%)	
occurrences (all)	14	72	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	5 / 147 (3.40%)	17 / 300 (5.67%)	
occurrences (all)	5	18	
Investigations			

Blood creatinine increased			
subjects affected / exposed	4 / 147 (2.72%)	15 / 300 (5.00%)	
occurrences (all)	5	26	
Neutrophil count decreased			
subjects affected / exposed	17 / 147 (11.56%)	2 / 300 (0.67%)	
occurrences (all)	26	2	
Weight decreased			
subjects affected / exposed	11 / 147 (7.48%)	22 / 300 (7.33%)	
occurrences (all)	13	30	
White blood cell count decreased			
subjects affected / exposed	15 / 147 (10.20%)	2 / 300 (0.67%)	
occurrences (all)	26	2	
Nervous system disorders			
Headache			
subjects affected / exposed	7 / 147 (4.76%)	15 / 300 (5.00%)	
occurrences (all)	7	20	
Dizziness			
subjects affected / exposed	8 / 147 (5.44%)	14 / 300 (4.67%)	
occurrences (all)	10	18	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	48 / 147 (32.65%)	50 / 300 (16.67%)	
occurrences (all)	70	57	
Leukopenia			
subjects affected / exposed	11 / 147 (7.48%)	3 / 300 (1.00%)	
occurrences (all)	15	3	
Neutropenia			
subjects affected / exposed	18 / 147 (12.24%)	2 / 300 (0.67%)	
occurrences (all)	39	3	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	28 / 147 (19.05%)	48 / 300 (16.00%)	
occurrences (all)	31	61	
Diarrhoea			
subjects affected / exposed	24 / 147 (16.33%)	40 / 300 (13.33%)	
occurrences (all)	45	57	
Nausea			

subjects affected / exposed	36 / 147 (24.49%)	32 / 300 (10.67%)	
occurrences (all)	54	40	
Vomiting			
subjects affected / exposed	23 / 147 (15.65%)	25 / 300 (8.33%)	
occurrences (all)	42	33	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	5 / 147 (3.40%)	30 / 300 (10.00%)	
occurrences (all)	7	44	
Pruritus			
subjects affected / exposed	3 / 147 (2.04%)	23 / 300 (7.67%)	
occurrences (all)	3	34	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 147 (0.00%)	19 / 300 (6.33%)	
occurrences (all)	0	22	
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	8 / 147 (5.44%)	12 / 300 (4.00%)	
occurrences (all)	9	12	
Back pain			
subjects affected / exposed	13 / 147 (8.84%)	25 / 300 (8.33%)	
occurrences (all)	14	29	
Arthralgia			
subjects affected / exposed	12 / 147 (8.16%)	28 / 300 (9.33%)	
occurrences (all)	15	36	
Infections and infestations			
Pneumonia			
subjects affected / exposed	5 / 147 (3.40%)	15 / 300 (5.00%)	
occurrences (all)	6	15	
Urinary tract infection			
subjects affected / exposed	12 / 147 (8.16%)	29 / 300 (9.67%)	
occurrences (all)	15	47	
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	32 / 147 (21.77%)	66 / 300 (22.00%)	
occurrences (all)	40	75	
Hypokalaemia			
subjects affected / exposed	2 / 147 (1.36%)	18 / 300 (6.00%)	
occurrences (all)	2	28	
Hyponatraemia			
subjects affected / exposed	7 / 147 (4.76%)	25 / 300 (8.33%)	
occurrences (all)	7	28	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 June 2017	This protocol was amended to 1. Exclude participants younger than 70 years with ECOG PS 0/1 in line with ESMO guidelines. 2. Include participants deemed 'unsuitable for any platinum doublet chemotherapy' as opposed to 'unsuitable for platinum containing therapy' to appropriately recruit cisplatin and carboplatin ineligible participants. 3. Increased frequency of on-treatment pregnancy tests and regular post-discontinuation visit pregnancy testing until at least 5 months after the last dose of atezolizumab or until at least 6 months after the last dose of chemotherapy.
16 January 2018	The protocol has been amended to include clarification of the key inclusion criteria in order to avoid the inclusion of too young participants with comorbidities or contraindications. The text on comparator chemotherapy administration guidelines has been amended to include both, administration per relevant local guidelines and per SmPC management as these may differ. The exclusion of participants with uncontrolled hypercalcaemia, including the exclusion of participants taking denosumab has been amended.
14 January 2019	The protocol has been amended to include the requirement for female participants of childbearing potential randomized to the atezolizumab arm to refrain from donating eggs to inclusion criteria.
19 December 2019	The protocol has been amended with the addition of an efficacy interim analysis with adequate power for the primary endpoint. OS and investigator-assessed PFS according to RECIST v1.1 in participants with PD-L1 expression defined by the SP263 IHC assay has been added as a secondary analysis. The list of atezolizumab risks has been updated to include myositis.
03 February 2021	The protocol has been amended to include severe cutaneous adverse reactions to the list of identified risks for atezolizumab. Text has been added to clarify that hemophagocytic lymphohistiocytosis (HLH) and macrophage activation syndrome (MAS) are considered potential risks for atezolizumab. List of identified risks for vinorelbine have been revised due to revisions of the Summary of Product Characteristics.
22 December 2021	The protocol has been amended to include a time limit for the final analysis as an alternative to the target 380 overall survival (OS) events. The adverse event management guidelines have been updated to align with the Atezolizumab Investigator's Brochure, Version 18.
09 May 2023	This protocol is amended to: 1. Include myelitis and facial paresis in list of identified risks. 2. Hemophagocytic lymphohistiocytosis (HLH) has been updated from a potential risk to an identified risk associated with atezolizumab.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported