Clinical trial results:
A Phase IIIb, Single Arm, Multicenter Study of Atezolizumab (Tecentriq) in Combination With Carboplatin Plus Etoposide to Investigate Safety and Efficacy in Patients With Untreated Extensive-stage Small Cell Lung Cancer - MAURIS

Summary

EudraCT number	2019-001146-17
Trial protocol	IT
Global end of trial date	13 July 2023

Results information

Result version number	v1 (current)
This version publication date	08 August 2024
First version publication date	08 August 2024

Trial information

Trial identification

Sponsor protocol code	ML41118

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04028050
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Hoffmann-La Roche AG
Sponsor organisation address	Grenzacherstrasse 124, Basel, Switzerland, CH-4070
Public contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.com
Scientific contact	F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	13 July 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	13 July 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety of atezolizumab in combination with carboplatin plus etoposide in patients with untreated extensive-stage small cell lung cancer (ES SCLC).

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	09 August 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Italy: 155
Worldwide total number of subjects	155
EEA total number of subjects	155

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)	72
From 65 to 84 years	83
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 25 locations in Italy.

Pre-assignment

Screening details:

A total of 155 participants were enrolled.

Period 1

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

Arms

Arm title	Atezolizumab + Carboplatin + Etoposide

Arm description:

Participants who received treatment until disease progression per RECIST v1.1, unacceptable toxicity, or symptomatic deterioration attributed to disease progression as determined by the investigator.

Arm type	Experimental
Investigational medicinal product name	Tecentriq
Investigational medicinal product code	
Other name	Atezolizumab RO5541267
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Fixed dose of 1200mg Q3W (1200 mg on Day 1 of each 21-day cycle during both the induction and the maintenance phase)

Investigational medicinal product name	Etoposide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

100 mg per square meter of body-surface area, administered intravenously on days 1 through 3 of each cycle. On Days 2 and 3, patients received etoposide alone.

Investigational medicinal product name	Carboplatino
Investigational medicinal product code	
Other name	Carboplatin
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

AUC 5mg per millilitre per minute, administered intravenously.

Number of subjects in period 1	Atezolizumab + Carboplatin + Etoposide
Started	155
Received at >1 dose of study treatment	154
Completed Induction Phase	120
Completed Maintenance Phase	136
Completed	19
Not completed	136
Adverse event, serious fatal	1
Consent withdrawn by subject	7
Physician Decision	2
Death	118
Progressive Disease	1
Unknown	1
Lost to follow-up	6

Baseline characteristics

Reporting groups	
Reporting group title	Atezolizumab + Carboplatin + Etoposide
Reporting group description:	
Participants who received treatment until disease progression per RECIST v1.1, unacceptable toxicity, or symptomatic deterioration attributed to disease progression as determined by the investigator.	

Reporting group values	Atezolizumab + Carboplatin + Etoposide	Total	
Number of subjects	155	155	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	72	72	
From 65-84 years	83	83	
85 years and over	0	0	
Age Continuous Units: Number			
arithmetic mean	65.1		
standard deviation	± 9.05	-	
Sex: Female, Male Units:			
Female	60	60	
Male	95	95	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	2	2	
Not Hispanic or Latino	153	153	
Unknown or Not Reported	0	0	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	0	0	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	0	0	
White	154	154	
More than one race	0	0	
Unknown or Not Reported	1	1	

End points

End points reporting groups

Reporting group title	Atezolizumab + Carboplatin + Etoposide

Reporting group description:

Participants who received treatment until disease progression per RECIST v1.1, unacceptable toxicity, or symptomatic deterioration attributed to disease progression as determined by the investigator.

Primary: Incidence of serious adverse events (SAEs) related to atezolizumab in combination with carboplatin plus etoposide treatment.

End point title	Incidence of serious adverse events (SAEs) related to atezolizumab in combination with carboplatin plus etoposide treatment.[1]

End point description:

Percentage of participants that experienced a serious adverse events (SAE) related to treatment.

End point type	Primary

End point timeframe:

From first dose of study treatment to 4 weeks after last dose of study treatment (3 years, 11 months).

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There was no hypothesis testing planned for this outcome measure. The analysis is descriptive in nature.

End point values	Atezolizumab + Carboplatin + Etoposide			
Subject group type	Reporting group			
Number of subjects analysed	154			
Units: Percentage of participants				
number (not applicable)	21.4			

Statistical analyses

No statistical analyses for this end point

Primary: Incidence of Serious and Non-Serious Immune Mediated Adverse Events (imAEs)

End point title	Incidence of Serious and Non-Serious Immune Mediated Adverse Events (imAEs)[2]

End point description:

Incidence of serious and non-serious immune-mediated adverse events (imAEs) related to treatment.

End point type	Primary

End point timeframe:

From first dose of study treatment to 4 weeks after last dose of study treatment (3 years, 11 months).

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There was no hypothesis testing planned for this outcome measure. The analysis is descriptive in nature.

End point values	Atezolizumab + Carboplatin + Etoposide			
Subject group type	Reporting group			
Number of subjects analysed	154[3]			
Units: Percentage of participants				
number (not applicable)	28.6			

Notes:

[3] - 1 participant withdrew before starting treatment

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS) Rate at 1 Year

End point title	Overall Survival (OS) Rate at 1 Year

End point description:

Overall Survival (OS) at 1 year, defined as the percentage of participants remaining alive at 1 year after initiation of study treatment.

End point type	Secondary

End point timeframe:

From initiation of study treatment to 1 Year (12 months).

End point values	Atezolizumab + Carboplatin + Etoposide			
Subject group type	Reporting group			
Number of subjects analysed	155			
Units: Percentage of participants				
number (confidence interval 95%)	45.5 (37.2 to 54.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS) Rate at 2 Years

End point title	Overall Survival (OS) Rate at 2 Years

End point description:

OS at 2 years, defined as the percentage of participants remaining alive at 2 years after initiation of study treatment.

End point type	Secondary

End point timeframe:

2 Years

End point values	Atezolizumab + Carboplatin + Etoposide			
Subject group type	Reporting group			
Number of subjects analysed	155			
Units: Percentage of participants				
number (confidence interval 95%)	17.1 (11.3 to 24.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS) Rate at 3 Years

End point title	Overall Survival (OS) Rate at 3 Years

End point description:

OS at 3 years, defined as the percentage of participants remaining alive at 3 years after initiation of study treatment.

End point type	Secondary

End point timeframe:

3 Years

End point values	Atezolizumab + Carboplatin + Etoposide			
Subject group type	Reporting group			
Number of subjects analysed	155			
Units: Percentage of participants				
number (confidence interval 95%)	14.5 (9.1 to 21.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Objective response rate (ORR)

End point title	Objective response rate (ORR)

End point description:

Objective response rate (ORR), is defined as the percentage of patients who attain complete response (CR) or partial response (PR) according to RECIST v1.

End point type	Secondary

End point timeframe:

3 years 11 months.

End point values	Atezolizumab + Carboplatin + Etoposide			
Subject group type	Reporting group			
Number of subjects analysed	155			
Units: Percentage of participants				
number (confidence interval 95%)				
Percentage of responders	72.3 (64.7 to 78.7)			
Percentage of non-responders	27.7 (21.3 to 35.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

Overall Survival (OS), defined as the time from initiation of study treatment to death from any cause.

End point type	Secondary

End point timeframe:

Overall Survival (OS) is defined as the time (in months) from initiation of study treatment to death from any cause. (3 years, 11 months)

End point values	Atezolizumab + Carboplatin + Etoposide			
Subject group type	Reporting group			
Number of subjects analysed	155			
Units: Months				
median (confidence interval 95%)	10.6 (9.8 to 13.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival (PFS)

End point title	Progression-Free Survival (PFS)

End point description:

Progression-Free Survival (PFS), is defined as the time (in months) from initiation of study treatment to the first occurrence of disease progression or death from any cause, whichever occurs first. PFS will be

calculated based on disease status evaluated by the investigator according to Response Evaluation Criteria in Solid Tumors, Version 1.1 (RECIST v1.1)

End point type	Secondary

End point timeframe:

From from initiation of study treatment to the first occurrence of disease progression or death from any cause, whichever occurs first (3 years, 11 months).

End point values	Atezolizumab + Carboplatin + Etoposide			
Subject group type	Reporting group			
Number of subjects analysed	155			
Units: Months				
median (confidence interval 95%)	5.5 (5.3 to 5.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR)

End point title	Duration of Response (DOR)

End point description:

Duration of response (DOR), defined as the time from initial response to disease progression or death among patients who have experienced a CR or PR (unconfirmed) during the study. Duration of response will be calculated based on disease status evaluated by the investigator according to RECIST v1.1.

End point type	Secondary

End point timeframe:

3 years 11 months.

End point values	Atezolizumab + Carboplatin + Etoposide			
Subject group type	Reporting group			
Number of subjects analysed	155			
Units: Months				
median (confidence interval 95%)				
Median DOR	4.2 (4.1 to 4.5)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study treatment to 4 weeks after last dose of study treatment (3 years, 11 months).

Adverse event reporting additional description:

AEs were reported for the safety population, defined as all those who received ≥1 dose of study treatment. There was one participant who withdrew from the study before receiving study treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	Atezolizumab + Carboplatin + Etoposide

Reporting group description:

Participants who received treatment until disease progression per RECIST v1.1, unacceptable toxicity, or symptomatic deterioration attributed to disease progression as determined by the investigator.

Serious adverse events	Atezolizumab + Carboplatin + Etoposide		
Total subjects affected by serious adverse events			
subjects affected / exposed	59 / 154 (38.31%)		
number of deaths (all causes)	120		
number of deaths resulting from adverse events	6		
Vascular disorders			
Arterial thrombosis			
subjects affected / exposed	1 / 154 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Inferior vena cava syndrome			
subjects affected / exposed	1 / 154 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 154 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Non-cardiac chest pain			

subjects affected / exposed	1 / 154 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	4 / 154 (2.60%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Pulmonary oedema			
subjects affected / exposed	1 / 154 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Pneumonitis			
subjects affected / exposed	1 / 154 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
White blood cell count decreased			
subjects affected / exposed	1 / 154 (0.65%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Platelet count decreased			
subjects affected / exposed	3 / 154 (1.95%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Neutrophil count decreased			
subjects affected / exposed	4 / 154 (2.60%)		
occurrences causally related to treatment / all	4 / 4		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Spinal fracture			

subjects affected / exposed	1 / 154 (0.65%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Fall				
subjects affected / exposed	1 / 154 (0.65%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Bradycardia				
subjects affected / exposed	1 / 154 (0.65%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
subjects affected / exposed	1 / 154 (0.65%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac failure				
subjects affected / exposed	2 / 154 (1.30%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 2			
Myocardial infarction				
subjects affected / exposed	1 / 154 (0.65%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Supraventricular tachycardia				
subjects affected / exposed	1 / 154 (0.65%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Atrial fibrillation				
subjects affected / exposed	1 / 154 (0.65%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				

Dysarthria			
subjects affected / exposed	1 / 154 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cognitive disorder			
subjects affected / exposed	1 / 154 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cerebrovascular accident			
subjects affected / exposed	1 / 154 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ataxia			
subjects affected / exposed	1 / 154 (0.65%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Encephalitis autoimmune			
subjects affected / exposed	1 / 154 (0.65%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Paraesthesia			
subjects affected / exposed	1 / 154 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spinal cord compression			
subjects affected / exposed	1 / 154 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	1 / 154 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			

Thrombocytopenia				
subjects affected / exposed	1 / 154 (0.65%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pancytopenia				
subjects affected / exposed	1 / 154 (0.65%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Neutropenias				
subjects affected / exposed	13 / 154 (8.44%)			
occurrences causally related to treatment / all	13 / 13			
deaths causally related to treatment / all	0 / 0			
Leukopenia				
subjects affected / exposed	1 / 154 (0.65%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Febrile neutropenia				
subjects affected / exposed	2 / 154 (1.30%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Eye disorders				
Diplopia				
subjects affected / exposed	1 / 154 (0.65%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Abdominal pain upper				
subjects affected / exposed	1 / 154 (0.65%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Constipation				
subjects affected / exposed	1 / 154 (0.65%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Diarrhoea			
subjects affected / exposed	2 / 154 (1.30%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 1		
Hepatobiliary disorders			
Hepatic failure			
subjects affected / exposed	1 / 154 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	1 / 154 (0.65%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	1 / 154 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Acute kidney injury			
subjects affected / exposed	3 / 154 (1.95%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Staphylococcal infections			
subjects affected / exposed	1 / 154 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Soft tissue infection			
subjects affected / exposed	1 / 154 (0.65%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis			

subjects affected / exposed	2 / 154 (1.30%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	2 / 154 (1.30%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	1 / 1		
Lung abscess			
subjects affected / exposed	1 / 154 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	3 / 154 (1.95%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	4 / 154 (2.60%)		
occurrences causally related to treatment / all	1 / 4		
deaths causally related to treatment / all	0 / 0		
Diabetic complication			
subjects affected / exposed	1 / 154 (0.65%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		

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

Non-serious adverse events	Atezolizumab + Carboplatin + Etoposide		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	130 / 154 (84.42%)		
Investigations			
Alanine aminotransferase increased			

subjects affected / exposed occurrences (all) Platelet count decreased subjects affected / exposed occurrences (all)	8 / 154 (5.19%) 8 15 / 154 (9.74%) 19		
Nervous system disorders Dysgeusia subjects affected / exposed occurrences (all)	 8 / 154 (5.19%) 8		
Blood and lymphatic system disorders Leukopenia subjects affected / exposed occurrences (all) Anaemia subjects affected / exposed occurrences (all) Thrombocytopenia subjects affected / exposed occurrences (all) Neutropenia subjects affected / exposed occurrences (all)	 9 / 154 (5.84%) 13 55 / 154 (35.71%) 70 18 / 154 (11.69%) 30 43 / 154 (27.92%) 60		
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all) Asthenia subjects affected / exposed occurrences (all)	 17 / 154 (11.04%) 18 35 / 154 (22.73%) 40 49 / 154 (31.82%) 66		
Gastrointestinal disorders Vomiting subjects affected / exposed occurrences (all)	 9 / 154 (5.84%) 11		

Nausea subjects affected / exposed occurrences (all)	20 / 154 (12.99%) 30		
Dyspepsia subjects affected / exposed occurrences (all)	8 / 154 (5.19%) 8		
Diarrhoea subjects affected / exposed occurrences (all)	18 / 154 (11.69%) 25		
Constipation subjects affected / exposed occurrences (all)	16 / 154 (10.39%) 23		
Abdominal pain upper subjects affected / exposed occurrences (all)	8 / 154 (5.19%) 8		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	14 / 154 (9.09%) 17		
Dyspnoea subjects affected / exposed occurrences (all)	14 / 154 (9.09%) 15		
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all)	12 / 154 (7.79%) 14		
Alopecia subjects affected / exposed occurrences (all)	11 / 154 (7.14%) 11		
Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all)	9 / 154 (5.84%) 12		
Musculoskeletal and connective tissue disorders Pain in extremity			

subjects affected / exposed occurrences (all)	10 / 154 (6.49%) 12		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	 8 / 154 (5.19%) 8		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 April 2020	Updates to Title and Eligibility Criteria
19 April 2021	Inclusion of interim analysis
23 June 2021	Appendix 5 update according to atezolizumab IB
31 March 2022	Updates to Secondary Outcome Measures
15 March 2023	Updates to AESI and Risks Associated with Atezolizumab

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported