Clinical trial results:
A Randomized, Multicenter, Open-Label Cross-Over Study to Evaluate Participant and Healthcare Professional Reported Preference for Subcutaneous Atezolizumab Compared With Intravenous Atezolizumab Formulation in Participants With Non–Small Cell Lung Cancer

Summary

EudraCT number	2021-004067-28
Trial protocol	IT ES FI LV
Global end of trial date	

Results information

Result version number	v1
This version publication date	06 November 2024
First version publication date	06 November 2024

Trial information

Trial identification

Sponsor protocol code	MO43576

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05171777
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
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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	Interim
Date of interim/final analysis	09 November 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 November 2023
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

The study aims to evaluate participant preference for atezolizumab subcutaneous (SC) compared with atezolizumab intravenous (IV).

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	04 April 2022
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	Argentina: 21
Country: Number of subjects enrolled	Brazil: 4
Country: Number of subjects enrolled	Canada: 8
Country: Number of subjects enrolled	Costa Rica: 8
Country: Number of subjects enrolled	Chile: 1
Country: Number of subjects enrolled	Finland: 8
Country: Number of subjects enrolled	Italy: 20
Country: Number of subjects enrolled	Korea, Democratic People's Republic of: 14
Country: Number of subjects enrolled	Latvia: 20
Country: Number of subjects enrolled	Poland: 28
Country: Number of subjects enrolled	Spain: 39
Country: Number of subjects enrolled	United States: 8
Worldwide total number of subjects	179
EEA total number of subjects	115

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	74
From 65 to 84 years	102
85 years and over	3

Subject disposition

Recruitment

Recruitment details:

Participants took part in the study across 37 investigative sites in 12 countries (Spain, Brazil, Finland, Italy, United States, Argentina, Canada, Republic of Korea, Costa Rica, Latvia, Poland, and Chile). This study is still ongoing.

Pre-assignment

Screening details:

A total of 179 participants with non-small cell lung cancer (NSCLC) were randomized in 1:1 ratio to Arm A (atezolizumab IV followed by atezolizumab SC) or Arm B (atezolizumab SC followed by atezolizumab IV). The study consists of two periods: Treatment Crossover Period, and Treatment Continuation Period.

Period 1

Period 1 title	Treatment Crossover Period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Crossover Atezolizumab IV/SC

Arm description:

Participants were administered atezolizumab, IV infusion, 1200 milligrams (mg), every 3 weeks (Q3W) for 3 cycles followed by atezolizumab, SC injections, 1875 mg, Q3W, for the next 3 cycles (cycle length=21 days) in the Treatment Crossover Period.

Arm type	Experimental
Investigational medicinal product name	Atezolizumab SC
Investigational medicinal product code	RO5541267
Other name	Tecentriq, MPDL3280A
Pharmaceutical forms	Concentrate for solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

Atezolizumab, 1875 mg, Q3W as SC on Day 1 of each 21-day cycle for 3 cycles or until loss of clinical benefit.

Investigational medicinal product name	Atezolizumab IV
Investigational medicinal product code	RO5541267
Other name	Tecentriq, MPDL3280A
Pharmaceutical forms	Concentrate for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Atezolizumab, 1200 mg, Q3W as IV infusion on Day 1 of each 21-day cycle for 3 cycles or until loss of clinical benefit.

Arm title	Crossover Atezolizumab SC/IV

Arm description:

Participants were administered atezolizumab, SC injections, 1875 mg, Q3W for 3 cycles followed by atezolizumab, IV, 1200 mg, Q3W, for the next 3 cycles (cycle length=21 days) in the Treatment Crossover Period.

Arm type	Experimental

Investigational medicinal product name	Atezolizumab IV
Investigational medicinal product code	RO5541267
Other name	Tecentriq, MPDL3280A
Pharmaceutical forms	Concentrate for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Atezolizumab, 1200 mg, Q3W as IV infusion on Day 1 of each 21-day cycle for 3 cycles or until loss of clinical benefit.

Investigational medicinal product name	Atezolizumab SC
Investigational medicinal product code	RO5541267
Other name	Tecentriq, MPDL3280A
Pharmaceutical forms	Concentrate for solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

Atezolizumab, 1875 mg, Q3W as SC on Day 1 of each 21-day cycle for 3 cycles or until loss of clinical benefit.

Number of subjects in period 1	Crossover Atezolizumab IV/SC	Crossover Atezolizumab SC/IV
Started	89	90
Completed	53	54
Not completed	36	36
Consent withdrawn by subject	4	4
Disease Relapse	-	1
Physician decision	-	1
Adverse Event	9	6
Death	5	5
Progressive Disease	13	9
Ongoing in the Crossover Treatment Period	3	6
Symptomatic Deterioration	-	1
Reason not Specified	2	1
Protocol deviation	-	2

Period 2

Period 2 title	Treatment Continuation Period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes

Arm title	Continuation Atezolizumab IV

Arm description:

After 6 cycles of Crossover Period, participants were given an option to choose between IV or SC administration of atezolizumab for the Treatment Continuation Period. Participants in this arm chose to continue treatment with atezolizumab IV, 1200 mg Q3W up to Cycle 16 for participants with early-stage NSCLC or until loss of clinical benefit for participants with advanced NSCLC.

Arm type	Experimental
Investigational medicinal product name	Atezolizumab IV
Investigational medicinal product code	RO5541267
Other name	Tecentriq, MPDL3280A
Pharmaceutical forms	Concentrate for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Atezolizumab, 1200 mg, Q3W as IV infusion on Day 1 of each 21-day cycle from cycle 6 for up to 16 cycles or until loss of clinical benefit.

Arm title	Continuation Atezolizumab SC

Arm description:

After 6 cycles of Crossover Period, participants were given an option to choose between IV or SC administration of atezolizumab for the Treatment Continuation Period. Participants in this arm chose to continue treatment with atezolizumab SC, 1875 mg Q3W up to Cycle 16 for participants with early-stage NSCLC or until loss of clinical benefit for participants with advanced NSCLC.

Arm type	Experimental
Investigational medicinal product name	Atezolizumab SC
Investigational medicinal product code	RO5541267
Other name	Tecentriq, MPDL3280A
Pharmaceutical forms	Concentrate for solution for injection/infusion
Routes of administration	Subcutaneous use

Dosage and administration details:

Atezolizumab, 1875 mg, Q3W as SC on Day 1 of each 21-day cycle from cycle 6 for up to 16 cycles or until loss of clinical benefit.

Number of subjects in period 2	Continuation Atezolizumab IV	Continuation Atezolizumab SC
Started	22	85
Completed	0	0
Not completed	22	85
Death	1	6
Ongoing in Continuation Treatment Period	21	79

Baseline characteristics

Reporting groups	
Reporting group title	Crossover Atezolizumab IV/SC
Reporting group description:	
Participants were administered atezolizumab, IV infusion, 1200 milligrams (mg), every 3 weeks (Q3W) for 3 cycles followed by atezolizumab, SC injections, 1875 mg, Q3W, for the next 3 cycles (cycle length=21 days) in the Treatment Crossover Period.	
Reporting group title	Crossover Atezolizumab SC/IV
Reporting group description:	
Participants were administered atezolizumab, SC injections, 1875 mg, Q3W for 3 cycles followed by atezolizumab, IV, 1200 mg, Q3W, for the next 3 cycles (cycle length=21 days) in the Treatment Crossover Period.	

Reporting group values	Crossover Atezolizumab IV/SC	Crossover Atezolizumab SC/IV	Total
Number of subjects	89	90	179
Age categorical			
Units: Subjects			
Age Continuous			
Units: years			
arithmetic mean	66.3	67.7	
standard deviation	± 9.2	± 9.4	-
Sex: Female, Male			
Units: participants			
Female	28	32	60
Male	61	58	119
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	1	2	3
Asian	5	8	13
Native Hawaiian or Other Pacific Islander	1	0	1
Black or African American	0	0	0
White	75	74	149
More than one race	0	0	0
Unknown or Not Reported	7	6	13
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	20	18	38
Not Hispanic or Latino	55	62	117
Unknown or Not Reported	14	10	24

End points reporting groups

Reporting group title	Crossover Atezolizumab IV/SC

Reporting group description:

Participants were administered atezolizumab, IV infusion, 1200 milligrams (mg), every 3 weeks (Q3W) for 3 cycles followed by atezolizumab, SC injections, 1875 mg, Q3W, for the next 3 cycles (cycle length=21 days) in the Treatment Crossover Period.

Reporting group title	Crossover Atezolizumab SC/IV

Reporting group description:

Participants were administered atezolizumab, SC injections, 1875 mg, Q3W for 3 cycles followed by atezolizumab, IV, 1200 mg, Q3W, for the next 3 cycles (cycle length=21 days) in the Treatment Crossover Period.

Reporting group title	Continuation Atezolizumab IV

Reporting group description:

After 6 cycles of Crossover Period, participants were given an option to choose between IV or SC administration of atezolizumab for the Treatment Continuation Period. Participants in this arm chose to continue treatment with atezolizumab IV, 1200 mg Q3W up to Cycle 16 for participants with early-stage NSCLC or until loss of clinical benefit for participants with advanced NSCLC.

Reporting group title	Continuation Atezolizumab SC

Reporting group description:

After 6 cycles of Crossover Period, participants were given an option to choose between IV or SC administration of atezolizumab for the Treatment Continuation Period. Participants in this arm chose to continue treatment with atezolizumab SC, 1875 mg Q3W up to Cycle 16 for participants with early-stage NSCLC or until loss of clinical benefit for participants with advanced NSCLC.

Subject analysis set title	Atezolizumab IV/SC (Cycles 1 to 3)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants were administered atezolizumab, IV infusion, 1200 mg, Q3W for Cycles 1 to 3 (cycle length=21 days) of the Treatment Crossover Period.

Subject analysis set title	Atezolizumab IV/SC (Cycles 4 to 6)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants were administered atezolizumab, SC injections, 1875 mg, Q3W for Cycles 4 to 6 (cycle length=21 days) of the Treatment Crossover Period.

Subject analysis set title	Atezolizumab SC/IV (Cycles 1 to 3)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants were administered atezolizumab, SC injections, 1875 mg, Q3W for Cycles 1 to 3 (cycle length=21 days) of the Treatment Crossover Period.

Subject analysis set title	Atezolizumab SC/IV (Cycles 4 to 6)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants were administered atezolizumab, IV infusion, 1200 mg, Q3W for Cycles 4 to 6 (cycle length=21 days) of the Treatment Crossover Period.

Subject analysis set title	Atezolizumab IV/SC
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants were administered atezolizumab, IV infusion, 1200 mg, Q3W for 3 cycles followed by atezolizumab, SC injections, 1875 mg, Q3W, for the next 3 cycles (cycle length=21 days) in the Treatment Crossover Period. HCPs who prepared and/or administered the IV/SC formulations completed the HCPQ questionnaire.

Subject analysis set title	Atezolizumab SC/IV
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants were administered atezolizumab, SC injections, 1875 mg, Q3W for 3 cycles followed by

atezolizumab, IV, 1200 mg, Q3W, for the next 3 cycles (cycle length=21 days) in the Treatment Crossover Period. HCPs who prepared and/or administered the IV/SC formulations completed the HCPQ questionnaire.

Subject analysis set title	Crossover + Continuation Periods (Atezolizumab IV/SC)
Subject analysis set type	Full analysis

Subject analysis set description:

Participants were administered atezolizumab, IV infusion, 1200 mg, Q3W for 3 cycles followed by atezolizumab, SC injections, 1875 mg, Q3W, for the next 3 cycles (cycle length=21 days) in the Treatment Crossover Period. After 6 cycles, participants could choose between IV or SC administration of atezolizumab in the Treatment Continuation Period. Participants continue to receive atezolizumab IV, 1200 mg or SC, 1875 mg Q3W up to Cycle 16 for participants with early-stage NSCLC or until loss of clinical benefit for participants with advanced NSCLC.

Subject analysis set title	Crossover + Continuation Periods (Atezolizumab SC/IV)
Subject analysis set type	Full analysis

Subject analysis set description:

Participants were administered atezolizumab, SC injections, 1875 mg, Q3W for 3 cycles followed by atezolizumab, IV, 1200 mg, Q3W, for the next 3 cycles (cycle length=21 days) in the Treatment Crossover Period. After 6 cycles, participants could choose between IV or SC administration of atezolizumab in the Treatment Continuation Period. Participants continue to receive atezolizumab IV, 1200 mg or SC, 1875 mg Q3W up to Cycle 16 for participants with early-stage NSCLC or until loss of clinical benefit, for participants with advanced NSCLC.

Primary: Percentage of Participants Who Preferred Atezolizumab SC to Atezolizumab IV Assessed Using Patient Preference Questionnaire (PPQ)

End point title	Percentage of Participants Who Preferred Atezolizumab SC to Atezolizumab IV Assessed Using Patient Preference Questionnaire (PPQ)[1]

End point description:

Participants preference was assessed based on the Question 1 (Q1) of PPQ. Q1 (All things considered, which route of administration did you prefer?) asks participants to report their preference for the route of administration (IV, SC, or no preference). A point estimate with associated 95% CI for the percentage of participants who preferred atezolizumab SC was calculated. Participants experiencing any of the following events: treatment withdrawal prior to eligibility for PPQ, or death without answering Q1 of PPQ, or treatment not started; were excluded from the analysis set. Participants who answered Q1 of the PPQ without having at least 2 consecutive administrations of treatment with each administration modality (SC and IV) were excluded from the analysis. Full Analysis Set (FAS) included all randomized participants. Number analyzed is the number of participants who answered Q1 of PPQ. Percentages have been rounded off.

End point type	Primary

End point timeframe:

Cycle 6 Day 1 (cycle length=21 days)

Notes:

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

End point values	Crossover Atezolizumab IV/SC	Crossover Atezolizumab SC/IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	63		
Units: percentage of participants				
number (confidence interval 95%)	71.67 (58.56 to 82.55)	69.84 (56.98 to 80.77)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants by Their Level of Satisfaction With Atezolizumab SC and Atezolizumab IV Assessed Using Therapy Administration Satisfaction Questionnaire – Subcutaneous (TASQ-SC) and Intravenous (TASQ-IV)

End point title	Number of Participants by Their Level of Satisfaction With Atezolizumab SC and Atezolizumab IV Assessed Using Therapy Administration Satisfaction Questionnaire – Subcutaneous (TASQ-SC) and Intravenous (TASQ-IV)

End point description:

TASQ=12-item, participant-reported questionnaire measuring the impact of each mode of treatment administration (TASQ-IV=IV treatment & TASQ-SC=SC treatment) on 5 domains: Physical Impact, Psychological Impact, Impact on Activities of Daily Living, Convenience, & Satisfaction. TASQ-IV/-SC was administered at treatment Cycles 3 & 6 according to order of treatment received per arm during Crossover Period. Participants satisfaction was assessed based on the Q1 of TASQ-IV/SC which asks participants about their satisfaction with respect to route of administration (very satisfied, satisfied, neither satisfied nor dissatisfied, dissatisfied, participant didn't answer question). TASQ- IV (Q1-How satisfied/dissatisfied were you with IV infusion?) & TASQ- SC (How satisfied or dissatisfied were you with SC injection?). FAS included all randomized participants. Number analyzed=number of participants with data available for analysis. n=number of participants who answered Q1 of TASQ IV/SC.

End point type	Secondary

End point timeframe:

Cycles 3 Day 1 and Cycle 6 Day 1 (cycle length=21 days)

End point values	Crossover Atezolizumab IV/SC	Crossover Atezolizumab SC/IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	74	71		
Units: participants				
TASQ- IV-Very Satisfied(n=74, 59)	25	10		
TASQ-IV-Satisfied(n=74, 59)	31	34		
TASQ-IV-Neither Satisfied/Dissatisfied(n=74,59)	17	11		
TASQ-IV-Dissatisfied(n=74, 59)	1	1		
TASQ-IV-Very Dissatisfied(n=74, 59)	0	3		
TASQ-IV-Participant didn't Answer(n=74,59)	0	0		
TASQ-SC-Very Satisfied(n=56, 71)	22	30		
TASQ-SC-Satisfied(n=56, 71)	21	36		
TASQ-SC-Neither Satisfied/Dissatisfied(n=56,71)	9	5		
TASQ-SC-Dissatisfied(n=56, 71)	3	0		
TASQ-SC-Very Dissatisfied(n=56, 71)	1	0		
TASQ-SC-Participant didn't Answer(n=56,71)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Treatment Preparation According to Healthcare Professionals (HCPs) Response to Perception of Time, Assessed Using Question 1 of HCPQs – Drug Preparation Area

End point title	Duration of Treatment Preparation According to Healthcare Professionals (HCPs) Response to Perception of Time, Assessed Using Question 1 of HCPQs – Drug Preparation Area

End point description:

The HCPQ- Drug Preparation Area Question 1 was completed by the HCPs within the pharmacy/drug preparation area where atezolizumab IV reconstitution or atezolizumab SC was prepared before the actual drug administration took place. The HCPQs were completed for every participant at each treatment cycle (Cycles 1–6, i.e., 3 cycles of atezolizumab IV followed by 3 cycles of atezolizumab SC or vice versa) of the treatment cross-over period. HCPs responded to the following parts of Question 1 that sought to evaluate the amount of time it took to prepare the IV infusion/SC injection of atezolizumab: "How long (in minutes) did it take to prepare the treatment for use?". Number analyzed included HCPs who completed Question 1 of the survey. "n"=number of HCPs who completed Question 1 of the survey at the specified treatment cycles.

End point type	Secondary

End point timeframe:

Day 1 of Cycles 1 to 6 (cycle length= 21 days)

End point values	Atezolizumab IV/SC	Atezolizumab SC/IV		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	84	83		
Units: minutes				
median (full range (min-max))				
Cycle 1 (n=84,83)	5.0 (1 to 40)	5.0 (1 to 45)		
Cycle 2 (n=80,80)	5.0 (1 to 40)	5.0 (1 to 35)		
Cycle 3 (n=72,74)	5.0 (1 to 45)	4.5 (1 to 40)		
Cycle 4 (n=67,71)	5.0 (1 to 35)	5.0 (1 to 50)		
Cycle 5 (n=62,64)	5.0 (1 to 35)	5.0 (1 to 59)		
Cycle 6 (n=56,60)	5.0 (1 to 35)	5.0 (1 to 36)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Select Atezolizumab SC for Treatment Continuation Period

End point title	Percentage of Participants Who Select Atezolizumab SC for Treatment Continuation Period

End point description:

At Cycle 6, Day 1, participants were expected to select the route of study treatment administration (SC or IV) they would like to receive during the Treatment Continuation Period (starting at Cycle 7). Percentage of participants who chose SC administration have been reported here. FAS included all randomized participants. Number analyzed is the number of participants with data available for analysis.

End point type	Secondary

End point timeframe:

Cycle 6 Day 1 (Cycle length=21 days)

End point values	Crossover Atezolizumab IV/SC	Crossover Atezolizumab SC/IV		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	53	54		
Units: percentage of participants				
number (not applicable)	79.2	79.6		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of HCPs by Their Response to Perception of Impact on Clinical Management and Clinical Efficiency of Atezolizumab SC and IV, Assessed Using Question 2 of HCPQ – Drug Preparation Area

End point title	Percentage of HCPs by Their Response to Perception of Impact on Clinical Management and Clinical Efficiency of Atezolizumab SC and IV, Assessed Using Question 2 of HCPQ – Drug Preparation Area

End point description:

HCPs within pharmacy/drug preparation area responded to HCPQ-Drug Preparation Area Q2 at Cycle 6: If all IV infusions are switched to SC, please indicate how strongly you agree/disagree with these statements: a=Staff will have increased availability for other tasks in pharmacy;b=Administrative procedures around atezolizumab (ATZ) SC will require less time;c=ATZ SC formulations will provide more flexibility for staff in managing their workload; d=Due to ready-to-use ATZ SC formulations, potential dosing errors will be avoided;e=Due to ready-to-use ATZ SC formulations, there will be less drug wastage;f=Without having to reconstitute the drug, less storage space for ATZ SC related supplies will be required in the pharmacy;g=Preparation procedures & associated time. staff time commitment will be reduced;h=It will ease drug administration for participants with difficult venous access. Number analyzed=HCPs who completed Q2 of survey at treatment Cycle 6. Percentages have been rounded off.

End point type	Secondary

End point timeframe:

Cycle 6 Day 1 (cycle length=21 days)

End point values	Atezolizumab IV/SC	Atezolizumab SC/IV		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	57	60		
Units: percentage of HCPs				
number (not applicable)				
a=Strongly Disagree (n=57,60)	7.0	10.0		
a=Disagree (n=57,60)	7.0	0		
a=Neutral (n=57,60)	21.1	31.7		
a=Agree (n=57,60)	24.6	20.0		
a=Strongly Agree (n=57,60)	31.6	25.0		
a=Not Applicable (n=57,60)	3.5	1.7		
a=Missing (n=57,60)	5.3	11.7		

b=Strongly Disagree (n=57,60)	7.0	10.0		
b=Disagree (n=57,60)	14.0	8.3		
b=Neutral (n=57,60)	29.8	28.3		
b=Agree (n=57,60)	12.3	18.3		
b=Strongly Agree (n=57,60)	24.6	16.7		
b=Not Applicable (n=57,60)	7.0	6.7		
b=Missing (n=57,60)	5.3	11.7		
c=Strongly Disagree (n=57,60)	0	0		
c=Disagree (n=57,60)	8.8	0		
c=Neutral (n=57,60)	29.8	53.3		
c=Agree (n=57,60)	26.3	18.3		
c=Strongly Agree (n=57,60)	26.3	15.0		
c=Not Applicable (n=57,60)	3.5	1.7		
c=Missing (n=57,60)	5.3	11.7		
d=Strongly Disagree (n=57,60)	12.3	20.0		
d=Disagree (n=57,60)	12.3	3.3		
d=Neutral (n=57,60)	22.8	30.0		
d=Agree (n=57,60)	15.8	18.3		
d=Strongly Agree (n=57,60)	28.1	15.0		
d=Not Applicable (n=57,60)	3.5	1.7		
d=Missing (n=57,60)	5.3	11.7		
e=Strongly Disagree (n=57,60)	1.8	0		
e=Disagree (n=57,60)	19.3	11.7		
e=Neutral (n=57,60)	14.0	26.7		
e=Agree (n=57,60)	29.8	38.3		
e=Strongly Agree (n=57,60)	26.3	10.0		
e=Not Applicable (n=57,60)	3.5	1.7		
e=Missing (n=57,60)	5.3	11.7		
f=Strongly Disagree (n=57,60)	0	1.7		
f=Disagree (n=57,60)	10.5	5.0		
f=Neutral (n=57,60)	33.3	46.7		
f=Agree (n=57,60)	21.1	20.0		
f=Strongly Agree (n=57,60)	26.3	8.3		
f=Not Applicable (n=57,60)	3.5	6.7		
f=Missing (n=57,60)	5.3	11.7		
g=Strongly Disagree (n=57,60)	5.3	11.7		
g=Disagree (n=57,60)	5.3	1.7		
g=Neutral (n=57,60)	26.3	36.7		
g=Agree (n=57,60)	26.3	21.7		
g=Strongly Agree (n=57,60)	28.1	15.0		
g=Not Applicable (n=57,60)	3.5	1.7		
g=Missing (n=57,60)	5.3	11.7		
h=Strongly Disagree (n=57,60)	0	0		
h=Disagree (n=57,60)	0	0		
h=Neutral (n=57,60)	10.5	15.0		
h=Agree (n=57,60)	40.4	38.3		
h=Strongly Agree (n=57,60)	28.1	25.0		
h=Not Applicable (n=57,60)	15.8	10.0		
h=Missing (n=57,60)	5.3	11.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of HCPs by Their Response to Perception of Time/Resource Use for Atezolizumab SC and Atezolizumab IV, Assessed Using Questions 3 and 4 of HCPQ - Drug Preparation Area

End point title	Percentage of HCPs by Their Response to Perception of Time/Resource Use for Atezolizumab SC and Atezolizumab IV, Assessed Using Questions 3 and 4 of HCPQ - Drug Preparation Area

End point description:

HCPs who prepared study treatment within the pharmacy/drug preparation area responded at Cycle 6 of the Treatment Crossover Period to the following HCPQ-Drug Preparation Area Questions 3 and 4: "Looking back over the Atezolizumab treatment sessions, please indicate based on your opinion which administration method: Q3. Was quickest from start to end of preparation to finish of administration (excluding observation period)?; Q4. Required less resource use for preparation and administration, for example nursing time, facility costs, equipment etc?" The four available response options were: Atezolizumab IV, Atezolizumab SC, No Difference, and Missing. Number analyzed included HCPs who completed Questions 3 and 4 of the survey at treatment Cycle 6. Percentages have been rounded off.

End point type	Secondary

End point timeframe:

Cycle 6 Day 1 (cycle length= 21 days)

End point values	Atezolizumab IV/SC	Atezolizumab SC/IV		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	57	60		
Units: percentage of HCPs				
number (not applicable)				
Q3=Atezolizumab SC (n=57,60)	71.9	58.3		
Q3=Atezolizumab IV (n=57,60)	0	0		
Q3=No Difference (n=57,60)	17.5	21.7		
Q3= Missing (n=57,60)	10.5	20.0		
Q4=Atezolizumab SC (n=57,60)	64.9	60.0		
Q4=Atezolizumab IV (n=57,60)	3.5	0		
Q4=No Difference (n=57,60)	21.1	20.0		
Q4=Missing (n=57,60)	10.5	20.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Treatment Administration Activities According to HCPs Response to Perception of Time, Assessed Using Question 1 of HCPQs – Treatment Room

End point title	Duration of Treatment Administration Activities According to HCPs Response to Perception of Time, Assessed Using Question 1 of HCPQs – Treatment Room

End point description:

HCPQ-Treatment Room Q1 was completed per cycle of Crossover Period by HCPs who administered treatment, responded to parts of Q1 that evaluates amount of time it took to complete activities related to treatment administration: If new IV access was needed for this cycle of treatment, please indicate what type of IV access was provided(central venous catheter(CVC),peripherally inserted central catheter(PICC),peripheral vein cannulation(PVC))&how long(mins)this took to set up(only for participants receiving IV treatment)?How long(mins)did it take to administer treatment,i.e.total infusion duration?How long(mins)was the participant in treatment room for in total? 99999=0 participants were analyzed at specified cycle. Durations with non-zero HCPs responders have been reported here. Number analyzed=HCPs who completed Q1 of survey. For the questions related to IV access, n=HCP responders for participants who required new IV access at a specified cycle & who completed Q1 of survey.

End point type	Secondary

End point timeframe:

Day 1 of Cycles 1 to 6 (cycle length=21 days)

End point values	Atezolizumab IV/SC	Atezolizumab SC/IV		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	87	86		
Units: minutes				
median (full range (min-max))				
Cycle 1:Duration of CVC set up?(n=1,0)	5.0 (5 to 5)	99999 (99999 to 99999)		
Cycle 1:Duration of PICC set up?(n=3,0)	30.0 (8 to 30)	99999 (99999 to 99999)		
Cycle 1:Duration of PVC set up?(n=62,0)	5.0 (1 to 70)	99999 (99999 to 99999)		
Cycle 1:How Long it Took to Administer?(n=85,86)	60.0 (10 to 120)	8.0 (5 to 75)		
Cycle1:How Long was Participant in Room?(n=85,86)	92.0 (35 to 390)	55.0 (10 to 260)		
Cycle 2:Duration of PICC set up?(n=3,0)	30.0 (5 to 35)	99999 (99999 to 99999)		
Cycle 2: Duration of PVC set up?(n=52,0)	5.0 (3 to 10)	99999 (99999 to 99999)		
Cycle 2:How Long it Took to Administer?(n=77,79)	30.0 (13 to 90)	6.0 (3 to 30)		
Cycle2: How Long was Participant in Room?(n=87,86)	75.0 (33 to 330)	41.0 (10 to 238)		
Cycle 3:Duration of CVC set up? (n=1,0)	61.0 (61 to 61)	99999 (99999 to 99999)		
Cycle 3: Duration of PICC set up?(n=4,0)	17.5 (5 to 30)	99999 (99999 to 99999)		
Cycle 3: Duration of PVC set up?(n=46,0)	5.0 (1 to 40)	99999 (99999 to 99999)		
Cycle3:How Long it Took to Administer?(n=72,75)	30.0 (20 to 66)	6.0 (3 to 15)		
Cycle3:How Long was Participant in Room?(n=72,75)	70.0 (35 to 323)	49.0 (5 to 128)		
Cycle 4:Duration of CVC set up?(n=0,1)	99999 (99999 to 99999)	10.0 (10 to 10)		

Cycle 4: Duration of PICC set up?(n=0,5)	99999 (99999 to 99999)	30.0 (10 to 60)		
Cycle 4:Duration of PVC set up?(n=0,49)	99999 (99999 to 99999)	5.0 (1 to 70)		
Cycle 4: How Long it Took to Administer? (n=68,70)	8.0 (5 to 73)	60.0 (15 to 90)		
Cycle4:How Long was Participant in Room?(n=87,86)	45.0 (10 to 320)	97.0 (20 to 360)		
Cycle 5:Duration of CVC set up? (n=0,1)	99999 (99999 to 99999)	5.0 (5 to 5)		
Cycle 5: Duration of PICC set up?(n=0,6)	99999 (99999 to 99999)	22.5 (7 to 51)		
Cycle 5: Duration of PVC set up?(n=0,46)	99999 (99999 to 99999)	5.0 (1 to 65)		
Cycle 5:How Long it Took to Administer?(n=61,65)	6.0 (1 to 15)	30.0 (8 to 60)		
Cycle5:How Long was Participant Room? (n=61,64)	35.0 (8 to 200)	71.0 (30 to 360)		
Cycle 6: Duration of PICC set up? (n=0,6)	99999 (99999 to 99999)	12.5 (5 to 30)		
Cycle 6: Duration of PVC set up?(n=0,40)	99999 (99999 to 99999)	5.0 (1 to 33)		
Cycle 6:How Long it Took to Administer? (n=58,60)	7.0 (1 to 35)	30.0 (8 to 63)		
Cycle6:How Long was Participant in Room? (n=58,60)	37.5 (9 to 240)	61.0 (14 to 380)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of HCPs by Their Response to Perception of Impact on Clinical Management and Clinical Efficiency of Atezolizumab SC and IV, Assessed Using Question 2 of HCPQ – Treatment Room

End point title	Percentage of HCPs by Their Response to Perception of Impact on Clinical Management and Clinical Efficiency of Atezolizumab SC and IV, Assessed Using Question 2 of HCPQ – Treatment Room

End point description:

HCPs who administered treatment responded to Q2: If all IV are switched to SC, please indicate how strongly you agree/disagree with following statements: a=Participants will be moved outside of infusion unit (IU) to receive SC injections; b=ATZ SC route will allow more flexible treatment scheduling; c=More participants will be treated in IU; d=Waiting list for IV treatment at IU will be reduced; e=Staff resources will be redistributed to other departments of hospital(i.e. less staffing required within IU); f=There will still be sufficient interaction time between HCP &participants (e.g. for participant education); g=Staff will spend more time for further professional education/development; h=Staff will dedicate more time to attending to administrative tasks for participants; i=Participants will spend less time in care unit; j=Administration by ATZ SC injection is preferred by participants. Number analyzed included HCPs who completed Q 2 of the survey at treatment Cycle 6.

End point type	Secondary

End point timeframe:

Cycle 6 Day 1 (cycle length=21 days)

End point values	Atezolizumab IV/SC	Atezolizumab SC/IV		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	58	61		
Units: percentage of HCPs				
number (not applicable)				
a=Strongly Disagree (n=61,89)	13.8	11.5		
a=Disagree (n=61,89)	15.5	23.0		
a=Neutral (n=61,89)	1.7	6.6		
a=Agree (n=61,89)	27.6	23.0		
a=Strongly Agree (n=61,89)	17.2	14.8		
a=Not Applicable (n=61,89)	10.3	1.6		
a=Missing (n=61,89)	13.8	19.7		
b=Strongly Disagree (n=61,89)	5.3	1.6		
b=Disagree (n=61,89)	19.0	14.8		
b=Neutral (n=61,89)	10.3	21.3		
b=Agree (n=61,89)	22.4	21.3		
b=Strongly Agree (n=61,89)	27.6	21.3		
b=Not Applicable (n=61,89)	1.7	0		
b=Missing (n=61,89)	13.8	19.7		
c=Strongly Disagree (n=61,89)	5.2	0		
c=Disagree (n=61,89)	15.5	16.4		
c=Neutral (n=61,89)	12.1	23.0		
c=Agree (n=61,89)	25.9	26.2		
c=Strongly Agree (n=61,89)	27.6	14.8		
c=Not Applicable (n=61,89)	0	0		
c=Missing (n=61,89)	13.8	19.7		
d=Strongly Disagree (n=61,89)	6.9	1.6		
d=Disagree (n=61,89)	5.2	6.6		
d=Neutral (n=61,89)	25.9	31.1		
d=Agree (n=61,89)	19.0	23.0		
d=Strongly Agree (n=61,89)	27.6	18.0		
d=Not Applicable (n=61,89)	1.7	0		
d=Missing (n=61,89)	13.8	19.7		
e=Strongly Disagree (n=61,89)	13.8	11.5		
e=Disagree (n=61,89)	8.6	14.8		
e=Neutral (n=61,89)	27.6	26.2		
e=Agree (n=61,89)	10.3	11.5		
e=Strongly Agree (n=61,89)	19.0	13.1		
e=Not Applicable (n=61,89)	6.9	3.3		
e=Missing (n=61,89)	13.8	19.7		
f=Strongly Disagree (n=61,89)	0	0		
f=Disagree (n=61,89)	17.2	11.5		
f=Neutral (n=61,89)	17.2	32.8		
f=Agree (n=61,89)	22.4	16.4		
f=Strongly Agree (n=61,89)	29.3	19.7		
f=Not Applicable (n=61,89)	0	0		
f=Missing (n=61,89)	13.8	19.7		
g=Strongly Disagree (n=61,89)	6.9	1.6		
g=Disagree (n=61,89)	12.1	11.5		
g=Neutral (n=61,89)	27.6	27.9		
g=Agree (n=61,89)	13.8	24.6		

g=Strongly Agree (n=61,89)	25.9	14.8		
g=Not Applicable (n=61,89)	0	0		
g=Missing (n=61,89)	13.8	19.7		
h=Strongly Disagree (n=61,89)	6.9	0		
h=Disagree (n=61,89)	17.2	24.6		
h=Neutral (n=61,89)	15.5	13.1		
h=Agree (n=61,89)	24.1	29.5		
h=Strongly Agree (n=61,89)	20.7	13.1		
h=Not Applicable (n=61,89)	1.7	0		
h=Missing (n=61,89)	13.8	19.7		
i=Strongly Disagree (n=61,89)	1.7	1.6		
i=Disagree (n=61,89)	5.2	4.9		
i=Neutral (n=61,89)	8.6	14.8		
i=Agree (n=61,89)	37.9	27.9		
i=Strongly Agree (n=61,89)	32.8	31.1		
i=Not Applicable (n=61,89)	0	0		
i=Missing (n=61,89)	13.8	19.7		
j=Strongly Disagree (n=61,89)	1.7	1.6		
j=Disagree (n=61,89)	0	3.3		
j=Neutral (n=61,89)	20.7	21.3		
j=Agree(n=61,89)	31.0	27.9		
j=Strongly Agree (n=61,89)	31.0	26.2		
j=Not Applicable (n=61,89)	1.7	0		
j=Missing (n=61,89)	13.8	19.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of HCPs by Their Response to Perception of Time/Resource Use and Convenience for Atezolizumab SC and Atezolizumab IV, Assessed Using Questions 3 to 7 of HCPQ - Treatment Room

End point title	Percentage of HCPs by Their Response to Perception of Time/Resource Use and Convenience for Atezolizumab SC and Atezolizumab IV, Assessed Using Questions 3 to 7 of HCPQ - Treatment Room

End point description:

HCPs who administered study treatment responded at Cycle 6 of the Treatment Cross-over Period to the following HCPQ-treatment room Questions 3 to 7: "Looking back over the atezolizumab treatment sessions, please indicate based on your opinion which administration method: Q3. Which method was most convenient for the participant? Q4. Which method was best for optimizing participant care in your centre? Q5. Which method took the least time from start to finish of administration? Q6. Which method required the least resource use for administration? Q7. Which method was preferred by participants? The five available response options were: Atezolizumab SC, Atezolizumab IV, No Difference, Unsure and Missing. Number analyzed included HCPs who completed Questions 3 to 7 of the survey at treatment Cycle 6. Percentages have been rounded off.

End point type	Secondary

End point timeframe:

Cycle 6 Day 1 (cycle length=21 days)

End point values	Atezolizumab IV/SC	Atezolizumab SC/IV		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	58	61		
Units: percentage of HCPs				
number (not applicable)				
Q3=Atezolizumab SC (n=58,61)	72.4	63.9		
Q3=Atezolizumab IV (n=58,61)	5.2	10.1		
Q3=No Difference (n=58,61)	6.9	8.4		
Q3=Unsure (n=58,61)	1.7	3.3		
Q3= Missing (n=58,61)	13.8	14.4		
Q4=Atezolizumab SC (n=58,61)	55.2	39.3		
Q4=Atezolizumab IV (n=58,61)	6.9	1.5		
Q4=No Difference (n=58,61)	20.7	31.1		
Q4=Unsure (n=58,61)	3.4	1.6		
Q4=Missing (n=58,61)	13.8	16.4		
Q5=Atezolizumab SC (n=58,61)	67.2	52.5		
Q5=Atezolizumab IV (n=58,61)	0	3.3		
Q5=No Difference (n=58,61)	17.2	27.9		
Q5=Unsure (n=58,61)	0	0		
Q5=Missing (n=58,61)	15.5	16.4		
Q6=Atezolizumab SC (n=58,61)	63.8	50.8		
Q6=Atezolizumab IV (n=58,61)	3.4	1.6		
Q6=No Difference (n=58,61)	19.0	31.1		
Q6=Unsure (n=58,61)	0	0		
Q6=Missing (n=58,61)	13.8	16.4		
Q7=Atezolizumab SC (n=58,61)	63.8	52.5		
Q7=Atezolizumab IV (n=58,61)	10.3	14.8		
Q7=No Difference (n=58,61)	3.4	1.6		
Q7=Unsure (n=58,61)	8.6	14.8		
Q7=Missing (n=58,61)	13.8	16.4		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of HCPs by Their Response to Perception of Time/Resource Use and Convenience for Atezolizumab SC and Atezolizumab IV, Assessed Using Questions 8 of HCPQ - Treatment Room

End point title	Percentage of HCPs by Their Response to Perception of Time/Resource Use and Convenience for Atezolizumab SC and Atezolizumab IV, Assessed Using Questions 8 of HCPQ - Treatment Room

End point description:

HCPs who administered study treatment responded at Cycle 6 of the Treatment Cross-over Period to the following HCPQ-treatment room Question 8: How frequently would you offer or recommend atezolizumab SC administration to your participants in the future? The four available response options were Always, Sometimes, Never and Missing. Number analyzed included HCPs who completed Question 8 of the survey at treatment Cycle 6. Percentages have been rounded off.

End point type	Secondary

End point timeframe:

Cycle 6 Day 1 (cycle length= 21 days)

End point values	Atezolizumab IV/SC	Atezolizumab SC/IV		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	58	61		
Units: percentage of HCPs				
number (not applicable)				
Q8=Always (n=58,61)	41.4	31.1		
Q8=Sometimes (n=58,61)	34.5	37.7		
Q8=Never (n=58,61)	10.3	14.8		
Q8=Missing (n=58,61)	13.8	16.4		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline Over Time in Health-related Quality of Life (HRQoL) Score as Assessed by GHS/QoL Scale of the EORTC-QLQ-C30

End point title	Change From Baseline Over Time in Health-related Quality of Life (HRQoL) Score as Assessed by GHS/QoL Scale of the EORTC-QLQ-C30

End point description:

EORTC QLQ-C30 consists of 30 questions that assess participant functioning (physical, emotional, role, cognitive, and social), symptom scales (fatigue, nausea and vomiting, pain), global health/QoL, and six single items (dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial difficulties). Change in HRQoL was assessed using participant responses to questions regarding Global Health Status (Q29: GHS; "How would you rate your overall health during the past week?") and QoL (Q30: QoL; "How would you rate your overall quality of life during the past week?") and were scored on a 7-point scale (1= Very poor to 7=Excellent). Using linear transformation, raw scores are standardized. Scores range from 0-100. A higher score indicates a better outcome. Data collection is ongoing for this endpoint and results will be disclosed within 1 year from Study Completion Date.

End point type	Secondary

End point timeframe:

From Day 1 up to 30 days after last study dose (up to approximately 2 years)

End point values	Crossover + Continuation Periods (Atezolizumab IV/SC)	Crossover + Continuation Periods (Atezolizumab SC/IV)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[2]	0[3]		
Units: score on a scale				
arithmetic mean (standard deviation)	()	()		

Notes:

[2] - Data collection is ongoing, and results will be disclosed within 1 year from Study Completion Date.

[3] - Data collection is ongoing, and results will be disclosed within 1 year from Study Completion Date.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline Over Time in Symptoms as Assessed by EORTC-QLQ-C30

End point title	Change From Baseline Over Time in Symptoms as Assessed by EORTC-QLQ-C30

End point description:

EORTC QLQ-C30 consists of 30 questions that assess five aspects of participant functioning (physical, emotional, role, cognitive, and social), three symptom scales (fatigue, nausea and vomiting, and pain), GHS and QoL, and six single items (dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial difficulties) with a recall period of the previous week. Scale scores can be obtained for the multi-item scales. The symptoms items are scored on a 4-point scale (1=Not at All to 4=Very Much). Scores are linearly transformed on a scale of 0 to 100, with a high score indicating worst functioning. Data collection is ongoing for this endpoint and results will be disclosed within 1 year from Study Completion Date.

End point type	Secondary

End point timeframe:

From Day 1 up to 30 days after last study dose (up to approximately 2 years)

End point values	Crossover + Continuation Periods (Atezolizumab IV/SC)	Crossover + Continuation Periods (Atezolizumab SC/IV)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[4]	0[5]		
Units: score on a scale				
arithmetic mean (standard deviation)	()	()		

Notes:

[4] - Data collection is ongoing, and results will be disclosed within 1 year from Study Completion Date.

[5] - Data collection is ongoing, and results will be disclosed within 1 year from Study Completion Date.

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline Over Time in Participant Functioning as Assessed by European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire – Core 30 (EORTC-QLQ-C30)

End point title	Change From Baseline Over Time in Participant Functioning as Assessed by European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire – Core 30 (EORTC-QLQ-C30)

End point description:

EORTC QLQ-C30 consists of 30 questions that assess five aspects of participant functioning (physical, emotional, role, cognitive, and social), three symptom scales (fatigue, nausea and vomiting, and pain), global health status (GHS) and quality of life (QoL), and six single items (dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial difficulties) with a recall period of the previous week. Scale scores can be obtained for the multi-item scales. The functioning items are scored on a 4-point scale (1=Not at All to 4=Very Much). Scores are linearly transformed on a scale of 0 to 100, with a high score indicating worst functioning. Data collection is ongoing for this endpoint and results will be disclosed within 1 year from Study Completion Date.

End point type	Secondary

End point timeframe:

From Day 1 up to 30 days after last study dose (up to approximately 2 years)

End point values	Crossover + Continuation Periods (Atezolizumab IV/SC)	Crossover + Continuation Periods (Atezolizumab SC/IV)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[6]	0[7]		
Units: score on a scale				
arithmetic mean (standard deviation)	()	()		

Notes:

[6] - Data collection is ongoing, and results will be disclosed within 1 year from Study Completion Date.

[7] - Data collection is ongoing, and results will be disclosed within 1 year from Study Completion Date.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Ongoing Clinical Benefit

End point title	Number of Participants With Ongoing Clinical Benefit

End point description:

Data collection is ongoing for this endpoint and results will be disclosed within 1 year from Study Completion Date.

End point type	Secondary

End point timeframe:

After Cycle 16 (cycle length=21 days)

End point values	Crossover + Continuation Periods (Atezolizumab IV/SC)	Crossover + Continuation Periods (Atezolizumab SC/IV)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[8]	0[9]		
Units: participants				

Notes:

[8] - Data collection is ongoing, and results will be disclosed within 1 year from Study Completion Date.

[9] - Data collection is ongoing, and results will be disclosed within 1 year from Study Completion Date.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Adverse Events (AEs)

End point title	Number of Participants With Adverse Events (AEs)

End point description:

An AE is untoward medical occurrence in participant administered a pharmaceutical product and

regardless of causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom/disease temporally associated with use of investigational product, whether or not considered related to investigational product. Data collection is ongoing for this endpoint and results will be disclosed within 1 year from Study Completion Date.

End point type	Secondary

End point timeframe:

Up to approximately 2 years

End point values	Crossover + Continuation Periods (Atezolizumab IV/SC)	Crossover + Continuation Periods (Atezolizumab SC/IV)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0[10]	0[11]		
Units: participants				

Notes:

[10] - Data collection is ongoing, and results will be disclosed within 1 year from Study Completion Date.
[11] - Data collection is ongoing, and results will be disclosed within 1 year from Study Completion Date.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With AEs During Treatment Crossover Period

End point title	Number of Participants With AEs During Treatment Crossover Period

End point description:

An AE is untoward medical occurrence in participant administered a pharmaceutical product and regardless of causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom/disease temporally associated with use of investigational product, whether or not considered related to investigational product. The safety of switching from atezolizumab SC to atezolizumab IV and from atezolizumab IV to atezolizumab SC is being assessed in this outcome measure. Safety evaluable population included all participants who received at least one dose of study treatment. In this analysis, participants were grouped by study arm and treatment period during the Crossover Period.

End point type	Secondary

End point timeframe:

From Cycle 1 Day 1 up to Cycle 3 Day 21; From Cycle 4 Day 1 up to Cycle 6 Day 21 (cycle length=21 days)

End point values	Atezolizumab IV/SC (Cycles 1 to 3)	Atezolizumab IV/SC (Cycles 4 to 6)	Atezolizumab SC/IV (Cycles 1 to 3)	Atezolizumab SC/IV (Cycles 4 to 6)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	89	69	86	71
Units: participants	56	27	47	38

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Cycle 1 Day 1 up to Cycle 6 Day 21 (cycle length=21 days)

Adverse event reporting additional description:

Safety evaluable population included all participants who received at least one dose of study treatment. This study is still ongoing. Safety data up to end of Treatment Crossover Period (i.e., end of Cycle 6) is presented here.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups

Reporting group title	Crossover Atezolizumab SC

Reporting group description:

Participants who were administered atezolizumab, SC injections, 1875 mg, Q3W for Cycles 1 to 3 or Cycles 4 to 6 (cycle length=21 days), depending on the sequence (IV/SC or SC/IV) they were assigned in the Treatment Crossover Period are reported in this arm.

Reporting group title	Crossover Atezolizumab IV

Reporting group description:

Participants who were administered atezolizumab, IV infusion, 1200 mg, Q3W in Cycles 1 to 3 or Cycles 4 to 6 (cycle length=21 days), depending on the sequence (IV/SC or SC/IV) they were assigned in the Treatment Crossover Period are reported in this arm.

Serious adverse events	Crossover Atezolizumab SC	Crossover Atezolizumab IV	
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 155 (8.39%)	15 / 160 (9.38%)	
number of deaths (all causes)	17	19	
number of deaths resulting from adverse events	1	0	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 155 (0.65%)	0 / 160 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infusion related reaction			
subjects affected / exposed	0 / 155 (0.00%)	2 / 160 (1.25%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Peripheral ischaemia			

subjects affected / exposed	0 / 155 (0.00%)	1 / 160 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shock			
subjects affected / exposed	1 / 155 (0.65%)	0 / 160 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hypertension			
subjects affected / exposed	1 / 155 (0.65%)	0 / 160 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac failure congestive			
subjects affected / exposed	1 / 155 (0.65%)	0 / 160 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	0 / 155 (0.00%)	1 / 160 (0.63%)	
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	1 / 155 (0.65%)	0 / 160 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac tamponade			
subjects affected / exposed	0 / 155 (0.00%)	1 / 160 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune-mediated myocarditis			
subjects affected / exposed	1 / 155 (0.65%)	0 / 160 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Autoimmune myocarditis			

subjects affected / exposed	1 / 155 (0.65%)	0 / 160 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	1 / 155 (0.65%)	1 / 160 (0.63%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Metabolic encephalopathy			
subjects affected / exposed	1 / 155 (0.65%)	0 / 160 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	1 / 155 (0.65%)	0 / 160 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Encephalopathy			
subjects affected / exposed	1 / 155 (0.65%)	0 / 160 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myasthenia gravis			
subjects affected / exposed	1 / 155 (0.65%)	0 / 160 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune-mediated encephalitis			
subjects affected / exposed	0 / 155 (0.00%)	2 / 160 (1.25%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 155 (0.00%)	1 / 160 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pain			
subjects affected / exposed	1 / 155 (0.65%)	0 / 160 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	1 / 155 (0.65%)	0 / 160 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	1 / 155 (0.65%)	0 / 160 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 155 (0.65%)	1 / 160 (0.63%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune-mediated enterocolitis			
subjects affected / exposed	0 / 155 (0.00%)	1 / 160 (0.63%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	1 / 155 (0.65%)	0 / 160 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
subjects affected / exposed	0 / 155 (0.00%)	1 / 160 (0.63%)	
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 / 155 (0.65%)	0 / 160 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	

Pulmonary embolism			
subjects affected / exposed	2 / 155 (1.29%)	0 / 160 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			
subjects affected / exposed	1 / 155 (0.65%)	0 / 160 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	1 / 155 (0.65%)	0 / 160 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute kidney injury			
subjects affected / exposed	1 / 155 (0.65%)	0 / 160 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Skin infection			
subjects affected / exposed	0 / 155 (0.00%)	1 / 160 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	0 / 155 (0.00%)	1 / 160 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	1 / 155 (0.65%)	0 / 160 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 155 (0.65%)	0 / 160 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Bronchitis			
subjects affected / exposed	0 / 155 (0.00%)	1 / 160 (0.63%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			
subjects affected / exposed	1 / 155 (0.65%)	2 / 160 (1.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	1 / 155 (0.65%)	0 / 160 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	1 / 155 (0.65%)	0 / 160 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Crossover Atezolizumab SC	Crossover Atezolizumab IV	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	40 / 155 (25.81%)	42 / 160 (26.25%)	
General disorders and administration site conditions			
Injection site reaction			
subjects affected / exposed	15 / 155 (9.68%)	0 / 160 (0.00%)	
occurrences (all)	23	0	
Fatigue			
subjects affected / exposed	7 / 155 (4.52%)	6 / 160 (3.75%)	
occurrences (all)	7	6	
Asthenia			
subjects affected / exposed	8 / 155 (5.16%)	9 / 160 (5.63%)	
occurrences (all)	9	9	
Gastrointestinal disorders			

Diarrhoea subjects affected / exposed occurrences (all)	10 / 155 (6.45%) 10	9 / 160 (5.63%) 11	
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all) Pruritus subjects affected / exposed occurrences (all)	 4 / 155 (2.58%) 5 8 / 155 (5.16%) 8	 9 / 160 (5.63%) 9 9 / 160 (5.63%) 9	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 February 2022	1. An error was corrected in the rational for the participant population regarding the dose to be used. 2. The eligibility requirement for a life expectancy of ≥18 weeks was updated to be in the opinion of the investigator. 3. A pathology report must also be provided if samples were sent to a central laboratory for EGFR and/or Anaplastic Lymphoma Kinase (ALK) testing. 4. Coagulation testing was only required at screening.
07 March 2023	1. The two exploratory immunogenicity objectives were merged into one streamlined objective encompassing the two. 2. The estimated sample size of the study was increased from approximately 140 participants to approximately 175 participants. 3. Endobronchial ultrasound-guided transbronchial needle aspiration was clarified to be an accepted sampling method for a right thoracotomy. 4. The definitions of the study populations and variables were replaced by cross-references to the Statistical Analysis Plan. 5. Steps 7 and 8 of the procedure in the event of a suspected anaphylactic reaction during study treatment infusion were removed because they are no longer required for atezolizumab. 6. The list of identified risks for atezolizumab was revised to include facial paresis, myelitis, pericardial disorders, and hemophagocytic lymphohistiocytosis. 7. The autoimmune diseases and immune deficiencies table in Appendix 7 was revised to include autoimmune myelitis.
27 February 2024	1. The list of approved indications for atezolizumab has been updated to include alveolar soft part sarcoma. 2. The safety follow-up duration was clarified to include safety follow-up every 90 days until the end of the trial 3. Personal identifiable information (i.e., name and telephone number) for the Medical Monitors has been removed from the protocol (front matter and Section 5.4.1). Medical Monitor contact information in Section 5.4.1 has been replaced with a sentence indicating that this information will be provided separately to sites.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported