



Clinical trial results:

A Phase Ib/II, Open-Label, Multicenter, Randomized Umbrella Study Evaluating the Efficacy and Safety of Multiple Treatment Combinations in Patients With Locally Advanced Squamous Cell Carcinoma of the Head and Neck (Morpheus-Head and Neck Cancer)

Summary

EudraCT number	2021-005712-62
Trial protocol	FR
Global end of trial date	15 August 2024

Results information

Result version number	v1
This version publication date	16 August 2025
First version publication date	16 August 2025

Trial information

Trial identification

Sponsor protocol code	CO43613
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05459129
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Hoffmann-La Roche
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	15 August 2024
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	15 August 2024
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main purpose of this study was to evaluate the efficacy of treatment combinations consisting of Atezolizumab + Tiragolumab (Atezo+Tira), & Atezolizumab + Tiragolumab + carboplatin/paclitaxel (CP), in treatment-naïve participants with locally advanced Stage III-IVA resectable squamous cell carcinoma of the head and neck (SCCHN).

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	13 April 2023
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	Israel: 2
Country: Number of subjects enrolled	Korea, Republic of: 3
Country: Number of subjects enrolled	United States: 7
Worldwide total number of subjects	12
EEA total number of subjects	0

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)	7
From 65 to 84 years	5

85 years and over	0
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Subject disposition

Recruitment

Recruitment details:

A total of 12 participants with locally advanced squamous cell carcinoma of the head and neck (SCCHN) took part in the study across 6 investigative sites in Israel, the Republic of Korea, and the United States from 12 April 2023 to 15 Aug 2024.

Pre-assignment

Screening details:

Participants were randomized to receive either Atezolizumab + Tiragolumab or Atezolizumab + Tiragolumab + carboplatin/ paclitaxel (CP). At the discretion of the investigator, participants started adjuvant therapy outside of this study, commencing between Week 10 and Week 13 and after treatment completion/discontinuation visit.

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 + Tiragolumab

Arm description:

Participants received atezolizumab, 1200 milligrams (mg) as intravenous (IV) infusion, along with tiragolumab, 600 mg, as IV infusion on Day 1 of each 21-day cycle for 2 cycles (6 weeks) until surgery (Week 7 \pm 1 week) or until unacceptable toxicity or loss of clinical benefit, whichever occurs first.

Arm type	Active comparator
Investigational medicinal product name	Tiragolumab
Investigational medicinal product code	RO7092284
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Tiragolumab, 600 mg, as IV infusion on Day 1 of each 21-day cycle.

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

Dosage and administration details:

Atezolizumab, 1200 mg, as IV infusion on Day 1 of each 21-day cycle.

Arm title	Atezolizumab + Tiragolumab + CP
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Arm description:

Participants received atezolizumab, 1200 mg as IV infusion, along with tiragolumab, 600 mg, as IV infusion; carboplatin, at a dose of area under the concentration-time curve (AUC) 5 milligrams/milliliters/minutes (mg/mL/min) as IV infusion and paclitaxel, 175 milligrams/meter square (mg/m²), as IV infusion on Day 1 of each 21-day cycle for 2 cycles (6 weeks) until surgery (Week 7 \pm 1 week) or until unacceptable toxicity or loss of clinical benefit, whichever occurs first.

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

Dosage and administration details:

Atezolizumab, 1200 mg, as IV infusion on Day 1 of each 21-day cycle.

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

Dosage and administration details:

Carboplatin at a dose of AUC 5 mg/mL/min Q3W, as IV infusion on Day 1 of each 21-day cycle.

Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	RO7092284
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Paclitaxel, 175 mg/m², as IV infusion on Day 1 of each 21-day cycle.

Investigational medicinal product name	Tiragolumab
Investigational medicinal product code	RO7092284
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Tiragolumab, 600 mg, as IV infusion on Day 1 of each 21-day cycle.

Number of subjects in period 1	Atezolizumab + Tiragolumab	Atezolizumab + Tiragolumab + CP
Started	6	6
Completed	0	0
Not completed	6	6
Study Terminated By Sponsor	5	6
Death	1	-

Baseline characteristics

Reporting groups

Reporting group title	Atezolizumab + Tiragolumab
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Reporting group description:

Participants received atezolizumab, 1200 milligrams (mg) as intravenous (IV) infusion, along with tiragolumab, 600 mg, as IV infusion on Day 1 of each 21-day cycle for 2 cycles (6 weeks) until surgery (Week 7 \pm 1 week) or until unacceptable toxicity or loss of clinical benefit, whichever occurs first.

Reporting group title	Atezolizumab + Tiragolumab + CP
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Reporting group description:

Participants received atezolizumab, 1200 mg as IV infusion, along with tiragolumab, 600 mg, as IV infusion; carboplatin, at a dose of area under the concentration-time curve (AUC) 5 milligrams/milliliters/minutes (mg/mL/min) as IV infusion and paclitaxel, 175 milligrams/meter square (mg/m²), as IV infusion on Day 1 of each 21-day cycle for 2 cycles (6 weeks) until surgery (Week 7 \pm 1 week) or until unacceptable toxicity or loss of clinical benefit, whichever occurs first.

Reporting group values	Atezolizumab + Tiragolumab	Atezolizumab + Tiragolumab + CP	Total
Number of subjects	6	6	12
Age categorical Units: Subjects			

Age Continuous Units: years arithmetic mean standard deviation	67.83 \pm 8.68	52.33 \pm 9.65	-
Sex: Female, Male Units: participants			
Female	1	2	3
Male	5	4	9
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	4	0	4
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	2	6	8
More than one race	0	0	0
Unknown or Not Reported	0	0	0
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	1	1
Not Hispanic or Latino	6	5	11
Unknown or Not Reported	0	0	0

End points

End points reporting groups

Reporting group title	Atezolizumab + Tiragolumab
Reporting group description: Participants received atezolizumab, 1200 milligrams (mg) as intravenous (IV) infusion, along with tiragolumab, 600 mg, as IV infusion on Day 1 of each 21-day cycle for 2 cycles (6 weeks) until surgery (Week 7 ± 1 week) or until unacceptable toxicity or loss of clinical benefit, whichever occurs first.	
Reporting group title	Atezolizumab + Tiragolumab + CP
Reporting group description: Participants received atezolizumab, 1200 mg as IV infusion, along with tiragolumab, 600 mg, as IV infusion; carboplatin, at a dose of area under the concentration-time curve (AUC) 5 milligrams/milliliters/minutes (mg/mL/min) as IV infusion and paclitaxel, 175 milligrams/meter square (mg/m ²), as IV infusion on Day 1 of each 21-day cycle for 2 cycles (6 weeks) until surgery (Week 7 ± 1 week) or until unacceptable toxicity or loss of clinical benefit, whichever occurs first.	

Primary: Percentage of Participants With Pathologic Complete Response (pCR) as Determined by Local Pathologic Review

End point title	Percentage of Participants With Pathologic Complete Response (pCR) as Determined by Local Pathologic Review
End point description: pCR was defined as the absence of any viable primary tumor at time of surgical resection, as determined by local pathologic review. The pCR rate was defined as the percentage of participants who achieved a pCR. pCR rate was calculated for each arm, along with the 95% confidence interval (CI) estimated using the Clopper-Pearson method and the 95% CI for difference in rates was estimated using the Wald method with continuity correction. Participants with missing or no pathologic response assessment were classified as non-responders. Percentages have been rounded off to the nearest whole number. Efficacy-evaluable population included all participants who received at least one dose of each drug for their assigned treatment regimen.	
End point type	Primary
End point timeframe: At the time of surgery (Week 7 ± 1 week)	

End point values	Atezolizumab + Tiragolumab	Atezolizumab + Tiragolumab + CP		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: percentage of participants				
number (confidence interval 95%)	16.7 (0.42 to 64.12)	50.0 (11.81 to 88.19)		

Statistical analyses

Statistical analysis title	Atezo+Tira vs Atezo+Tira+ CP
Comparison groups	Atezolizumab + Tiragolumab v Atezolizumab + Tiragolumab + CP

Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in pCR Rates
Point estimate	33.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-33.23
upper limit	99.9

Secondary: Pathologic Response Rate (pRR) as Determined by Local Pathologic Review

End point title	Pathologic Response Rate (pRR) as Determined by Local Pathologic Review
End point description:	
pRR was defined as the percentage of participants with a pCR, major pathological response (mPR), and pathological partial response (pPR). pCR was defined as the absence of any viable primary tumor at time of surgical resection, as determined by local pathologic review. mPR was defined as $\leq 10\%$ residual viable tumor at the time of surgical resection in the primary tumor. pPR was defined as $\leq 50\%$ residual viable tumor at the time of surgical resection in the primary tumor. pRR was calculated for each arm, along with the 95% CI, estimated using the Clopper-Pearson method, and the 95% CI for the difference in rates was estimated using the Wald method with continuity correction. Percentages have been rounded off to the nearest whole number. Efficacy-evaluable population included all participants who received at least one dose of each drug for their assigned treatment regimen.	
End point type	Secondary
End point timeframe:	
At the time of surgery (Week 7 \pm 1 week)	

End point values	Atezolizumab + Tiragolumab	Atezolizumab + Tiragolumab + CP		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: percentage of participants				
number (confidence interval 95%)	66.7 (22.28 to 95.67)	100 (54.07 to 100.00)		

Statistical analyses

Statistical analysis title	Atezo+Tira vs Atezo+Tira+ CP
Comparison groups	Atezolizumab + Tiragolumab v Atezolizumab + Tiragolumab + CP

Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in pRR
Point estimate	33.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-21.05
upper limit	87.72

Secondary: Event-Free Survival (EFS)

End point title	Event-Free Survival (EFS)
End point description:	
EFS=time from randomization to disease progression (PD) that precludes surgery, as determined by the investigator according to Response Evaluation Criteria in Solid Tumors, Version 1.1 (RECIST v1.1); local, regional/distant disease recurrence/death from any cause, whichever occurs first. PD=at least 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum of diameters at prior timepoints (including baseline), & must also demonstrate an absolute increase of ≥ 5 millimeters (mm). Kaplan-Meier method was used to estimate the median for EFS, & 95% CIs was constructed using Brookmeyer & Crowley method. Efficacy-evaluable population. 9999=Median & upper limit of 95 % CI was not estimable due to insufficient number of participants with events. Due to the early termination of the study, the limited sample size and follow-up time no meaningful conclusions can be made in terms of median EFS per arm or HR between the arms.	
End point type	Secondary
End point timeframe:	
From randomization to PD disease recurrence or death (Up to 9.2 months)	

End point values	Atezolizumab + Tiragolumab	Atezolizumab + Tiragolumab + CP		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6 ^[1]	6 ^[2]		
Units: months				
median (confidence interval 95%)	9999 (2.96 to 9999)	9999 (4.30 to 9999)		

Notes:

[1] - Median & 95% CI couldn't be estimated due to insufficient events as study was terminated prematurely

[2] - Median & 95% CI couldn't be estimated due to insufficient events as study was terminated prematurely

Statistical analyses

Statistical analysis title	Atezo+Tira vs Atezo+Tira+ CP
Statistical analysis description:	
HR was estimated by Cox regression. Due to the early termination of the study, the limited sample size and follow-up time no meaningful conclusions can be made in terms of median EFS per arm or HR between the arms.	
Comparison groups	Atezolizumab + Tiragolumab v Atezolizumab + Tiragolumab + CP

Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.11
upper limit	3.91

Secondary: Relapse-Free Survival (RFS)

End point title	Relapse-Free Survival (RFS)
End point description:	
RFS=time from surgery to first documented recurrence of disease/death from any cause. Recurrent disease= local, regional, or distant recurrence: local recurrence was defined as tumor regrowth within 2 centimeter (cm) of the primary lesion's tumor bed; regional recurrence as any nodal or non-nodal tumor lesions that are more than 2 cm from the primary lesion but are not beyond regional nodal basin; distant recurrence as any non-local/non-regional recurrence. Kaplan-Meier method was used to estimate the median for RFS, and 95% CIs was constructed using Brookmeyer and Crowley method. Adjuvant-evaluable population included all participants who received at least 1 dose of each drug and who completed surgery. 9999= Median and upper limit of 95 % CI was not estimable due to insufficient number of participants with events. Due to early termination of study, the limited sample size and follow-up time no meaningful conclusions can be made in terms of median RFS per arm or HR between the arms	
End point type	Secondary
End point timeframe:	
From surgery (scheduled at Week 7 ± 1 week) to first documented disease recurrence or death (up to 7.6 months)	

End point values	Atezolizumab + Tiragolumab	Atezolizumab + Tiragolumab + CP		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	6		
Units: months				
median (confidence interval 95%)	9999 (0.99 to 9999)	9999 (2.79 to 9999)		

Statistical analyses

Statistical analysis title	Atezo+Tira vs Atezo+Tira+ CP
Statistical analysis description:	
HR was estimated by Cox regression. Due to the early termination of the study, the limited sample size and follow-up time no meaningful conclusions can be made in terms of media RFS per arm or HR between the arms.	
Comparison groups	Atezolizumab + Tiragolumab v Atezolizumab + Tiragolumab + CP

Number of subjects included in analysis	11
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.13
upper limit	6.43

Secondary: Objective Response Rate (ORR)

End point title	Objective Response Rate (ORR)
End point description:	
<p>ORR was defined as the percentage of participants with an objective tumor response of complete response (CR) or partial response (PR) as determined by the investigator using RECIST v.1.1. CR was defined as the disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) have a reduction in short axis to <10 millimeters (mm). PR was defined as at least a 30% decrease in the sum of diameters (SOD) of target lesions, taking as reference the baseline SOD. ORR was calculated for each arm, along with 95% CIs, using the Clopper-Pearson method and the 95% CI for difference in rates was estimated using the Wald method with continuity correction. Participants with missing or no response assessments were classified as non-responders. Percentages have been rounded off to the nearest whole number.</p>	
End point type	Secondary
End point timeframe:	
Prior to surgery (up to Week 6)	

End point values	Atezolizumab + Tiragolumab	Atezolizumab + Tiragolumab + CP		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: percentage of participants				
number (confidence interval 95%)	33.3 (4.33 to 77.72)	50.0 (11.81 to 88.19)		

Statistical analyses

Statistical analysis title	Atezo+Tira vs Atezo+Tira+ CP
Comparison groups	Atezolizumab + Tiragolumab + CP v Atezolizumab + Tiragolumab

Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in ORR
Point estimate	16.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	-54.99
upper limit	88.32

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)
End point description:	
OS was defined as the time from randomization to death from any cause. Data from participants who were still alive at the time of OS analysis were censored at the last date they were known to be alive. Kaplan-Meier method was used to estimate the median for OS, and 95% CIs was constructed using Brookmeyer and Crowley method. Efficacy-evaluable population included all who received at least one dose of each drug for their assigned treatment regimen. 9999=median and upper limit of 95 % CI was not estimable due to insufficient number of participants with events. Due to the early termination of the study, the limited sample size and follow-up time no meaningful conclusions can be made in terms of median OS and no further OS analysis are reported.	
End point type	Secondary
End point timeframe:	
From randomization to death from any cause or last known to be alive (Up to 9.2 months)	

End point values	Atezolizumab + Tiragolumab	Atezolizumab + Tiragolumab + CP		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: months				
median (confidence interval 95%)	9999 (9999 to 9999)	9999 (9999 to 9999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Landmark EFS Rate

End point title	Landmark EFS Rate
End point description:	
EFS=time from randomization to PD that precludes surgery,as determined by investigator per RECIST v1.1; local, regional, or distant disease recurrence/death from any cause, whichever occurs first. EFS rate=percentage of participants who are event-free at the specified timepoints. PD=at least a 20% increase in SOD of target lesions, taking as reference smallest SOD at prior timepoints (including baseline) & must also demonstrate an absolute increase of ≥ 5 mm. EFS rates were estimated for each study arm using the Kaplan-Meier method, with 95% CIs calculated using Greenwood's formula.	

Efficacy-evaluable population. 'n' per timepoint are unique number of participants out of all the assessed participants who remain at risk for an EFS event at that timepoint. Different participants may have contributed data for each timepoint. 999=No participants were analyzed for this timepoint. Due to early termination of study, limited sample size & follow-up time no meaningful conclusions were made.

End point type	Secondary
End point timeframe:	
3 Months, 6 Months, and 1 Year	

End point values	Atezolizumab + Tiragolumab	Atezolizumab + Tiragolumab + CP		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: percentage of participants				
number (confidence interval 95%)				
3 Months (n=4, 5)	66.67 (28.95 to 100.00)	83.33 (53.51 to 100.00)		
6 Months (n=4, 4)	66.67 (28.95 to 100.00)	66.67 (28.95 to 100.00)		
1 Year (n=0, 0)	999 (999 to 999)	999 (999 to 999)		

Statistical analyses

Statistical analysis title	Atezo+Tira vs Atezo+Tira+ CP (6 Months)
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Statistical analysis description:

Due to the early termination of the study, the limited sample size and follow-up time no meaningful conclusions can be made.

Comparison groups	Atezolizumab + Tiragolumab v Atezolizumab + Tiragolumab + CP
Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in Event Free Rate
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-53.34
upper limit	53.34

Statistical analysis title	Atezo+Tira vs Atezo+Tira+ CP (3Months)
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Statistical analysis description:

Due to the early termination of the study, the limited sample size and follow-up time no meaningful conclusions can be made.

Comparison groups	Atezolizumab + Tiragolumab v Atezolizumab + Tiragolumab + CP
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Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in Event Free Rate
Point estimate	16.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	-31.42
upper limit	64.75

Secondary: Landmark RFS Rate

End point title	Landmark RFS Rate
End point description:	
RFS=time from surgery to the first documented recurrence of disease/death from any cause. RFS rate=percentage of participants who are event-free at specified timepoints. Recurrent disease=local, regional, or distant recurrence: local recurrence= tumor regrowth within 2 cm of the primary lesion's tumor bed; regional recurrence= any nodal/non-nodal tumor lesions > 2 cm from primary lesion but are not beyond the regional nodal basin; distant recurrence= any non-local/non-regional recurrence. RFS rates were estimated using KM method, with 95% CIs calculated using Greenwood's formula. Adjuvant-evaluable population. 'n' per timepoint are unique number of participants out of all the assessed participants who remain at risk for an RFS event at that timepoint. Different participants may have contributed data for each timepoint.999=No participants were analyzed for this timepoint. Due to early termination of study, limited sample size & follow-up time no meaningful conclusions were made.	
End point type	Secondary
End point timeframe:	
3 Months, 6 Months, and 1 Year	

End point values	Atezolizumab + Tiragolumab	Atezolizumab + Tiragolumab + CP		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	6		
Units: percentage of participants				
number (confidence interval 95%)				
3 Months (n=4, 4)	80.00 (44.94 to 100.00)	66.67 (28.95 to 100.00)		
6 Months (n=2, 2)	60.00 (17.06 to 100.00)	66.67 (28.95 to 100.00)		
1 Year (n=0, 0)	999 (999 to 999)	999 (999 to 999)		

Statistical analyses

Statistical analysis title	Atezo+Tira vs Atezo+Tira+ CP (6 Months)
Statistical analysis description:	
Due to the early termination of the study, the limited sample size and follow-up time no meaningful conclusions can be made .	

Comparison groups	Atezolizumab + Tiragolumab v Atezolizumab + Tiragolumab + CP
Number of subjects included in analysis	11
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in Event Free Rate
Point estimate	6.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	-50.49
upper limit	63.82

Statistical analysis title	Atezo+Tira vs Atezo+Tira+ CP (3 Months)
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Statistical analysis description:

Due to the early termination of the study, the limited sample size and follow-up time no meaningful conclusions can be made .

Comparison groups	Atezolizumab + Tiragolumab v Atezolizumab + Tiragolumab + CP
Number of subjects included in analysis	11
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Difference in Event Free Rate
Point estimate	-13.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-64.83
upper limit	38.16

Secondary: Landmark OS Rate

End point title	Landmark OS Rate
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End point description:

OS was defined as the time from randomization to death from any cause. OS rate was defined as the percentage of participants who are event-free at the specified timepoints. Landmark OS rates were estimated for each study arm using the Kaplan-Meier method, with 95% CIs calculated through the use of Greenwood's formula. Efficacy-evaluable population included all participants who received at least one dose of each drug for their assigned treatment regimen. 'n' per timepoint are unique number of participants out of all the assessed participants who remain at risk for an OS event at that timepoint. Different participants may have contributed data for each timepoint. 999=No participants were analyzed for this timepoint. Due to the early termination of the study, the limited sample size and follow-up time no meaningful conclusions can be made .

End point type	Secondary
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End point timeframe:

3 Months, 6 Months, and 1 Year

End point values	Atezolizumab + Tiragolumab	Atezolizumab + Tiragolumab + CP		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: percentage of participants				
number (confidence interval 95%)				
3 Months (n=6, 6)	100.00 (100.00 to 100.00)	100.00 (100.00 to 100.00)		
6 Months (n=5, 6)	83.33 (53.51 to 100.00)	100.00 (100.00 to 100.00)		
1 Year (n= 0,0)	999 (999 to 999)	999 (999 to 999)		

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)
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End point description:

An AE was any untoward medical occurrence in a participant administered a pharmaceutical product and which does not necessarily have to have a causal relationship with the treatment. An AE can therefore be any unfavorable and unintended sign (including abnormal laboratory values or abnormal clinical test results), symptoms, or disease temporally associated with the use of a pharmaceutical product, whether or not considered related to the pharmaceutical product. Safety-evaluable population included all randomized participants who received any amount of dose of any component of the study treatment.

End point type	Secondary
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End point timeframe:

From initiation of study treatment up to 135 days after the final dose of study treatment (up to 5.1 months)

End point values	Atezolizumab + Tiragolumab	Atezolizumab + Tiragolumab + CP		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: participants	6	6		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Immune-Related AEs Grade ≥ 3

End point title	Number of Participants with Immune-Related AEs Grade ≥ 3
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End point description:

An AE was any untoward medical occurrence in a participant administered a pharmaceutical product and which does not necessarily have to have a causal relationship with the treatment. An AE can therefore be any unfavorable and unintended sign (including abnormal laboratory values or abnormal clinical test results), symptoms, or disease temporally associated with the use of a pharmaceutical product, whether or not considered related to the pharmaceutical product. Grade 3 AEs were defined as severe or medically significant, but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; or limiting self-care activities of daily living. Safety-evaluable population included all randomized participants who received any amount of dose of any component of the study treatment.

End point type	Secondary
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End point timeframe:

Up to 12 weeks

End point values	Atezolizumab + Tiragolumab	Atezolizumab + Tiragolumab + CP		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of Delayed Surgery Due to Treatment-Related AEs

End point title	Rate of Delayed Surgery Due to Treatment-Related AEs
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End point description:

Rate of delayed surgery due to treatment related AEs was defined as the percentage of participants for whom surgery was delayed due to treatment-related AEs for 2 weeks. An AE was any untoward medical occurrence in a participant administered a pharmaceutical product and which does not necessarily have to have a causal relationship with the treatment. An AE can therefore be any unfavorable and unintended sign (including abnormal laboratory values or abnormal clinical test results), symptoms, or disease temporally associated with the use of a pharmaceutical product, whether or not considered related to the pharmaceutical product. Safety-evaluable population included all randomized participants who received any amount of dose of any component of the study treatment.

End point type	Secondary
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End point timeframe:

Delay after the planned time of surgery (scheduled at Week 7 \pm 1 week) up to 2 weeks (up to Week 9)

End point values	Atezolizumab + Tiragolumab	Atezolizumab + Tiragolumab + CP		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Delayed Surgery Due to Treatment-Related AEs

End point title	Duration of Delayed Surgery Due to Treatment-Related AEs
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End point description:

Duration of surgery delay due to treatment related AEs was calculated on the participants for whom surgery was delayed due to treatment-related AEs for 2 weeks. An AE was any untoward medical occurrence in a participant administered a pharmaceutical product and which does not necessarily have to have a causal relationship with the treatment. An AE can therefore be any unfavorable and unintended sign (including abnormal laboratory values or abnormal clinical test results), symptoms, or disease temporally associated with the use of a pharmaceutical product, whether or not considered related to the pharmaceutical product. Safety-evaluable population included all randomized participants who received any amount of dose of any component of the study treatment. Number analyzed= participants with delayed surgery due to treatment related AEs.

End point type	Secondary
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End point timeframe:

Delay after the planned time of surgery (scheduled at Week 7 \pm 1 week) up to 2 weeks (up to Week 9)

End point values	Atezolizumab + Tiragolumab	Atezolizumab + Tiragolumab + CP		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[3]	0 ^[4]		
Units: weeks				
arithmetic mean (standard deviation)	()	()		

Notes:

[3] - No participants had surgery delayed due to treatment-related AEs.

[4] - No participants had surgery delayed due to treatment-related AEs.

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of Surgical Complications as Assessed According to the Clavien-Dindo Surgical Classification

End point title	Rate of Surgical Complications as Assessed According to the Clavien-Dindo Surgical Classification
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End point description:

Surgical complications were scored according to Clavien-Dindo surgical classification. Complication rates for every grade were scored for participants who underwent complete lymph node dissection (CLND). Surgical complications per Clavien-Dindo are classified into following grades: Grade I=Any complication not needing pharmacological treatment/surgical, endoscopic & radiological interventions. Grade II=Complications requiring pharmacological treatment with drugs/blood transfusions & total parenteral nutrition. Grade III=Complications that require surgical, endoscopic/radiological intervention with (Grade IIIb) or without (Grade IIIa) general anesthesia. Grade IV=Life-threatening complications requiring intensive care unit (ICU) management, which may be single organ (Grade IVa) or multiorgan

(Grade IVb) dysfunction. Grade V=Complications that might cause death of participant. Only non-zero categorical data was reported. Number analyzed=number of participants who underwent surgery.

End point type	Secondary
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End point timeframe:

From Surgery (Week 7 \pm 1 week) up to 5.1 months

End point values	Atezolizumab + Tiragolumab	Atezolizumab + Tiragolumab + CP		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	6		
Units: percentage of participants				
Grade IIIb	0	1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From initiation of study treatment up to 135 after the final dose of study treatment (up to 5.1 months)

All-cause mortality: Up to 9.2 months

Adverse event reporting additional description:

Safety-evaluable population included all randomized participants who received any amount of dose of any component of the study treatment.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	27.0
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Reporting groups

Reporting group title	Atezolizumab + Tiragolumab + CP
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Reporting group description:

Participants received atezolizumab, 1200 mg as IV infusion, along with tiragolumab, 600 mg, as IV infusion; carboplatin, at a dose of AUC 5 mg/mL/min as IV infusion and paclitaxel, 175 mg/m², as IV infusion on Day 1 of each 21-day cycle for 2 cycles (6 weeks) until surgery (Week 7 ± 1 week) or until unacceptable toxicity or loss of clinical benefit, whichever occurs first.

Reporting group title	Atezolizumab + Tiragolumab
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Reporting group description:

Participants received atezolizumab, 1200 mg as IV infusion, along with tiragolumab, 600 mg, as IV infusion on Day 1 of each 21-day cycle for 2 cycles (6 weeks) until surgery (Week 7 ± 1 week) or until unacceptable toxicity or loss of clinical benefit, whichever occurs first.

Serious adverse events	Atezolizumab + Tiragolumab + CP	Atezolizumab + Tiragolumab	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 6 (50.00%)	1 / 6 (16.67%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Arterial injury			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Vascular rupture			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			

Febrile neutropenia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspiration			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (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			
Appendicitis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Atezolizumab + Tiragolumab + CP	Atezolizumab + Tiragolumab	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	6 / 6 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Peritumoural oedema			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	2	
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Fatigue			
subjects affected / exposed	2 / 6 (33.33%)	1 / 6 (16.67%)	
occurrences (all)	4	2	
Influenza like illness			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Localised oedema			
subjects affected / exposed	1 / 6 (16.67%)	1 / 6 (16.67%)	
occurrences (all)	1	1	
Pyrexia			
subjects affected / exposed	2 / 6 (33.33%)	0 / 6 (0.00%)	
occurrences (all)	3	0	
Pain			
subjects affected / exposed	1 / 6 (16.67%)	1 / 6 (16.67%)	
occurrences (all)	1	1	
Oedema			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Mucosal inflammation			
subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	

Malaise subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0	
Respiratory, thoracic and mediastinal disorders Productive cough subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all) Cough subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0 1 / 6 (16.67%) 1 1 / 6 (16.67%) 1	1 / 6 (16.67%) 1 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0	
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all) Anxiety subjects affected / exposed occurrences (all) Sleep disorder subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1 1 / 6 (16.67%) 1 1 / 6 (16.67%) 1	0 / 6 (0.00%) 0 0 / 6 (0.00%) 0 0 / 6 (0.00%) 0	
Investigations Neutrophil count decreased subjects affected / exposed occurrences (all) Weight decreased subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1 0 / 6 (0.00%) 0	0 / 6 (0.00%) 0 1 / 6 (16.67%) 1	
Injury, poisoning and procedural complications Radiation skin injury subjects affected / exposed occurrences (all) Procedural pain	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0	

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	2 / 6 (33.33%) 2	
Wound dehiscence subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0	
Cardiac disorders Tachycardia subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0	
Nervous system disorders Peripheral sensory neuropathy subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 6 (16.67%) 1	
Paraesthesia subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0	
Hypoaesthesia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 6 (16.67%) 1	
Headache subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0	
Dysgeusia subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0	
Dizziness subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0	
Eye disorders Swelling of eyelid subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0	
Gastrointestinal disorders Mouth swelling subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0	
Mouth haemorrhage			

subjects affected / exposed	0 / 6 (0.00%)	1 / 6 (16.67%)	
occurrences (all)	0	1	
Hypoaesthesia oral			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Dysphagia			
subjects affected / exposed	2 / 6 (33.33%)	1 / 6 (16.67%)	
occurrences (all)	2	1	
Dyspepsia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 6 (16.67%)	
occurrences (all)	1	1	
Dry mouth			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Diarrhoea			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	2	0	
Constipation			
subjects affected / exposed	2 / 6 (33.33%)	0 / 6 (0.00%)	
occurrences (all)	3	0	
Tongue ulceration			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	1	0	
Oral pain			
subjects affected / exposed	3 / 6 (50.00%)	1 / 6 (16.67%)	
occurrences (all)	3	2	
Nausea			
subjects affected / exposed	4 / 6 (66.67%)	2 / 6 (33.33%)	
occurrences (all)	7	2	
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	1 / 6 (16.67%)	0 / 6 (0.00%)	
occurrences (all)	2	0	
Rash			
subjects affected / exposed	1 / 6 (16.67%)	1 / 6 (16.67%)	
occurrences (all)	1	1	

Pruritus subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0	
Alopecia subjects affected / exposed occurrences (all)	2 / 6 (33.33%) 2	0 / 6 (0.00%) 0	
Dermatitis subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	1 / 6 (16.67%) 1	
Renal and urinary disorders Dysuria subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 6 (16.67%) 1	
Musculoskeletal and connective tissue disorders Spondylolisthesis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 6 (16.67%) 1	
Arthralgia subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0	
Muscle spasms subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0	
Myalgia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 6 (16.67%) 1	
Infections and infestations Otitis externa subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 6 (16.67%) 1	
Oral candidiasis subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0	
Enterobacter infection subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0	

Candida infection subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0	
Appendicitis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 6 (16.67%) 1	
Metabolism and nutrition disorders			
Decreased appetite subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 6 (16.67%) 1	
Hypercalcaemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 6 (16.67%) 1	
Hyponatraemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 6 (16.67%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 December 2022	<ul style="list-style-type: none">• Treatment arms Atezolizumab monotherapy arm and Atezolizumab +Tira + immune-modulating stereotactic body radiotherapy (iSBRT) arm were removed.• EU Clinical Trials (CT) number was added to align with Clinical Trials Regulation and other guidelines• The landmark event-free survival, landmark relapse-free survival, and landmark overall survival were considered part of secondary efficacy endpoints instead of exploratory efficacy endpoints according to study design. Exploratory efficacy endpoints section was removed.• The total number of participants to enroll in the study was adapted to the removal of Atezo monotherapy and Atezo +Tira + iSBRT arms.• HIV inclusion criteria were modified to include more eligible population• Additional minor changes were made to improve clarity and consistency

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported