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 Melanoma (Morpheus-Melanoma)

Summary

EudraCT number	2021-002147-29
Trial protocol	ES FR IT NL
Global end of trial date	28 May 2024

Results information

Result version number	v1 (current)
This version publication date	06 June 2025
First version publication date	06 June 2025

Trial information

Trial identification

Sponsor protocol code	BO43328

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05116202
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, genentech@druginfo.com
Scientific contact	Medical Communications, Hoffmann-La Roche, +41 616878333, genentech@druginfo.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	28 May 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 May 2024
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

This study evaluated the efficacy, safety, and pharmacokinetics of treatment combinations in cancer immunotherapy (CIT)-naive participants with resectable Stage III melanoma (Cohort 1) and in participants with Stage IV melanoma (Cohort 2).

Protection of trial subjects:

All study participants were required to read and sign an informed consent form (ICF).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 February 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	Australia: 45
Country: Number of subjects enrolled	Spain: 6
Country: Number of subjects enrolled	France: 25
Country: Number of subjects enrolled	Italy: 16
Country: Number of subjects enrolled	United States: 18
Worldwide total number of subjects	110
EEA total number of subjects	47

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)	62

From 65 to 84 years	48
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants took part in the study across 14 investigative sites in 5 countries: the United States, Italy, France, Spain, and Australia. A total of 110 participants with resectable Stage III melanoma and Stage IV melanoma took part in Cohort 1 and Cohort 2, respectively.

Pre-assignment

Screening details:

A total of 6 treatment arms were planned in Cohort 1 and 102 participants were enrolled in only 4 arms. The study was closed before the Cohort 1 arms tobemstomig 600 milligrams (mg), and tobemstomig 600 mg + tiragolumab were opened. 8 participants were enrolled in 1 arm in Cohort 2.

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	Cohort 1: Nivolumab + Ipilimumab (Control)

Arm description:

Participants received nivolumab 3 milligrams/kilograms (mg/kg) intravenously (IV) and ipilimumab 1 mg/kg IV on Day 1 of each 21-day cycle for 2 cycles (6 weeks) until surgery (Week 7) or until unacceptable toxicity or loss of clinical benefit, whichever occurs first. Post-surgery at the discretion of the investigator, participants started either adjuvant therapy or an observation phase from Week 13.

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

Dosage and administration details:

Participants received nivolumab, 3 mg/kg, IV, on Day 1 of each 21 Day cycle.

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

Dosage and administration details:

Participants received ipilimumab, 1 mg/kg, IV, on Day 1 of each 21 Day cycle.

Arm title	Cohort 1: Tobemstomig 2100 mg

Arm description:

Participants received a fixed dose of tobemstomig 2100 mg IV on Day 1 of each 21-day cycle for 2 cycles (6 weeks) until surgery (Week 7) or until unacceptable toxicity or loss of clinical benefit, whichever occurs first. Post-surgery at the discretion of the investigator, participants started either adjuvant therapy or an observation phase from Week 13.

Arm type	Experimental

Investigational medicinal product name	Tobemstomig
Investigational medicinal product code	RO7247669
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received tobemstomig, 2100 mg, IV on Day 1 of each 21 Day cycle.

Arm title	Cohort 1: Atezolizumab + Tiragolumab

Arm description:

Participants received atezolizumab 1200 mg IV and tiragolumab 600 mg IV on Day 1 of each 21-day cycle for 2 cycles (6 weeks) until surgery (Week 7) or until unacceptable toxicity or loss of clinical benefit, whichever occurs first. Post-surgery at the discretion of the investigator, participants started either adjuvant therapy or an observation phase from Week 13.

Arm type	Experimental
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:

Participants received tiragolumab, 600 mg, IV on Day 1 of each 21 Day cycle.

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

Dosage and administration details:

Participants received atezolizumab, 1200 mg, IV on Day 1 of each 21 Day cycle.

Arm title	Cohort 1: Tobemstomig + Tiragolumab

Arm description:

Participants received tobemstomig 2100 mg IV and tiragolumab 600 mg IV on Day 1 of each 21-day cycle for 2 cycles (6 weeks) until surgery (Week 7) or until unacceptable toxicity or loss of clinical benefit, whichever occurs first. Post-surgery at the discretion of the investigator, participants started either adjuvant therapy or an observation phase from Week 13.

Arm type	Experimental
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:

Participants received tiragolumab, 600 mg, IV on Day 1 of each 21 Day cycle.

Investigational medicinal product name	Tobemstomig
Investigational medicinal product code	RO7247669
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received tobemstomig, 2100 mg, IV on Day 1 of each 21 Day cycle.

Arm title	Cohort 2: Tobemstomig + Tiragolumab

Arm description:

Participants received tobemstomig 2100 mg IV and tiragolumab 600 mg IV on Day 1 of each 21-day cycle until unacceptable toxicity or loss of clinical benefit as determined by the investigator after an

integrated assessment of radiographic and biochemical data, local biopsy results (if available), and clinical status.

Arm type	Experimental
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:

Participants received tiragolumab, 600 mg, IV on Day 1 of each 21 Day cycle.

Investigational medicinal product name	Tobemstomig
Investigational medicinal product code	RO7247669
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received tobemstomig, 2100 mg, IV on Day 1 of each 21 Day cycle.

Number of subjects in period 1	Cohort 1: Nivolumab + Ipilimumab (Control)	Cohort 1: Tobemstomig 2100 mg	Cohort 1: Atezolizumab + Tiragolumab
Started	22	40	20
Completed	0	0	0
Not completed	22	40	20
Consent withdrawn by subject	-	1	1
Death	1	1	2
Study Terminated by Sponsor	21	38	17
Lost to follow-up	-	-	-

Number of subjects in period 1	Cohort 1: Tobemstomig + Tiragolumab	Cohort 2: Tobemstomig + Tiragolumab
Started	20	8
Completed	0	0
Not completed	20	8
Consent withdrawn by subject	1	1
Death	1	5
Study Terminated by Sponsor	18	-
Lost to follow-up	-	2

Baseline characteristics

Reporting groups	
Reporting group title	Cohort 1: Nivolumab + Ipilimumab (Control)
Reporting group description:	
Participants received nivolumab 3 milligrams/kilograms (mg/kg) intravenously (IV) and ipilimumab 1 mg/kg IV on Day 1 of each 21-day cycle for 2 cycles (6 weeks) until surgery (Week 7) or until unacceptable toxicity or loss of clinical benefit, whichever occurs first. Post-surgery at the discretion of the investigator, participants started either adjuvant therapy or an observation phase from Week 13.	
Reporting group title	Cohort 1: Tobemstomig 2100 mg
Reporting group description:	
Participants received a fixed dose of tobemstomig 2100 mg IV on Day 1 of each 21-day cycle for 2 cycles (6 weeks) until surgery (Week 7) or until unacceptable toxicity or loss of clinical benefit, whichever occurs first. Post-surgery at the discretion of the investigator, participants started either adjuvant therapy or an observation phase from Week 13.	
Reporting group title	Cohort 1: Atezolizumab + Tiragolumab
Reporting group description:	
Participants received atezolizumab 1200 mg IV and tiragolumab 600 mg IV on Day 1 of each 21-day cycle for 2 cycles (6 weeks) until surgery (Week 7) or until unacceptable toxicity or loss of clinical benefit, whichever occurs first. Post-surgery at the discretion of the investigator, participants started either adjuvant therapy or an observation phase from Week 13.	
Reporting group title	Cohort 1: Tobemstomig + Tiragolumab
Reporting group description:	
Participants received tobemstomig 2100 mg IV and tiragolumab 600 mg IV on Day 1 of each 21-day cycle for 2 cycles (6 weeks) until surgery (Week 7) or until unacceptable toxicity or loss of clinical benefit, whichever occurs first. Post-surgery at the discretion of the investigator, participants started either adjuvant therapy or an observation phase from Week 13.	
Reporting group title	Cohort 2: Tobemstomig + Tiragolumab
Reporting group description:	
Participants received tobemstomig 2100 mg IV and tiragolumab 600 mg IV on Day 1 of each 21-day cycle until unacceptable toxicity or loss of clinical benefit as determined by the investigator after an integrated assessment of radiographic and biochemical data, local biopsy results (if available), and clinical status.	

Reporting group values	Cohort 1: Nivolumab + Ipilimumab (Control)	Cohort 1: Tobemstomig 2100 mg	Cohort 1: Atezolizumab + Tiragolumab
Number of subjects	22	40	20
Age categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	55.05	64.10	58.90
standard deviation	± 16.03	± 10.97	± 14.10
Sex: Female, Male Units: participants			
Female	11	9	8
Male	11	31	12
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0

Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	15	35	14
More than one race	0	0	0
Unknown or Not Reported	7	5	6
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1	0	0
Not Hispanic or Latino	13	29	10
Unknown or Not Reported	8	11	10

Reporting group values	Cohort 1: Tobemstomig + Tiragolumab	Cohort 2: Tobemstomig + Tiragolumab	Total
Number of subjects	20	8	110
Age categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	59.15	52.63	
standard deviation	± 10.69	± 14.22	-
Sex: Female, Male Units: participants			
Female	6	3	37
Male	14	5	73
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	0	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	0	1
White	14	8	86
More than one race	0	0	0
Unknown or Not Reported	4	0	22
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	0	1
Not Hispanic or Latino	16	8	76
Unknown or Not Reported	4	0	33

End points

End points reporting groups

Reporting group title	Cohort 1: Nivolumab + Ipilimumab (Control)
Reporting group description:	
Participants received nivolumab 3 milligrams/kilograms (mg/kg) intravenously (IV) and ipilimumab 1 mg/kg IV on Day 1 of each 21-day cycle for 2 cycles (6 weeks) until surgery (Week 7) or until unacceptable toxicity or loss of clinical benefit, whichever occurs first. Post-surgery at the discretion of the investigator, participants started either adjuvant therapy or an observation phase from Week 13.	
Reporting group title	Cohort 1: Tobemstomig 2100 mg
Reporting group description:	
Participants received a fixed dose of tobemstomig 2100 mg IV on Day 1 of each 21-day cycle for 2 cycles (6 weeks) until surgery (Week 7) or until unacceptable toxicity or loss of clinical benefit, whichever occurs first. Post-surgery at the discretion of the investigator, participants started either adjuvant therapy or an observation phase from Week 13.	
Reporting group title	Cohort 1: Atezolizumab + Tiragolumab
Reporting group description:	
Participants received atezolizumab 1200 mg IV and tiragolumab 600 mg IV on Day 1 of each 21-day cycle for 2 cycles (6 weeks) until surgery (Week 7) or until unacceptable toxicity or loss of clinical benefit, whichever occurs first. Post-surgery at the discretion of the investigator, participants started either adjuvant therapy or an observation phase from Week 13.	
Reporting group title	Cohort 1: Tobemstomig + Tiragolumab
Reporting group description:	
Participants received tobemstomig 2100 mg IV and tiragolumab 600 mg IV on Day 1 of each 21-day cycle for 2 cycles (6 weeks) until surgery (Week 7) or until unacceptable toxicity or loss of clinical benefit, whichever occurs first. Post-surgery at the discretion of the investigator, participants started either adjuvant therapy or an observation phase from Week 13.	
Reporting group title	Cohort 2: Tobemstomig + Tiragolumab
Reporting group description:	
Participants received tobemstomig 2100 mg IV and tiragolumab 600 mg IV on Day 1 of each 21-day cycle until unacceptable toxicity or loss of clinical benefit as determined by the investigator after an integrated assessment of radiographic and biochemical data, local biopsy results (if available), and clinical status.	

Primary: Pathologic Response Rate (pRR) for Cohort 1 as Determined by Independent Pathologic Review

End point title	Pathologic Response Rate (pRR) for Cohort 1 as Determined by Independent Pathologic Review[1]
End point description:	
pRR was defined as the percentage of participants with pathologic complete response (pCR), pathologic near complete response (pnCR), and pathologic partial response (pPR) as determined by an independent pathologic review. pCR was defined as a complete absence of viable tumor cells, pnCR as > 0 to ≤ 10% of viable tumor cells, and pPR was defined as > 10 to ≤ 50% of viable tumor cells in the dissected lymph node. Participants with missing or no pathologic response assessment, including participants who did not proceed to complete lymph node dissection (CLND), were classified as non-responders. pRR was calculated for each arm along with 95% confidence intervals (CIs) using Clopper-Pearson method. The difference in pRR between the experimental arms and the control arm was calculated, along with 95% CIs using the Wald method with continuity correction. Efficacy-evaluable population=all participants in Cohort 1 who received at least 1 dose of each drug for their assigned treatment regimen.	
End point type	Primary
End point timeframe:	
Time of surgery (scheduled at Week 7)	
Notes:	
[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: No statistical analysis for this end point.	

End point values	Cohort 1: Nivolumab + Ipilimumab (Control)	Cohort 1: Tobemstomig 2100 mg	Cohort 1: Atezolizumab + Tiragolumab	Cohort 1: Tobemstomig + Tiragolumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22	40	20	20
Units: percentage of participants				
number (confidence interval 95%)	77.3 (54.63 to 92.18)	80.0 (64.35 to 90.95)	45.0 (23.06 to 68.47)	60.0 (36.05 to 80.88)

Statistical analyses

Statistical analysis title	Nivo + Ipi vs Tobe 2100 mg
Comparison groups	Cohort 1: Tobemstomig 2100 mg v Cohort 1: Nivolumab + Ipilimumab (Control)
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in pRR
Point estimate	2.73
Confidence interval	
level	95 %
sides	2-sided
lower limit	-22.25
upper limit	27.7

Statistical analysis title	Nivo + Ipi vs Tobe + Tira
Comparison groups	Cohort 1: Nivolumab + Ipilimumab (Control) v Cohort 1: Tobemstomig + Tiragolumab
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in pRR
Point estimate	-17.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-49.75
upper limit	15.21

Statistical analysis title	Nivo + Ipi vs Atezo + Tira
Comparison groups	Cohort 1: Nivolumab + Ipilimumab (Control) v Cohort 1: Atezolizumab + Tiragolumab

Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in pRR
Point estimate	-32.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-65.01
upper limit	0.46

Primary: Objective Response Rate (ORR) for Cohort 2 as Determined by the Investigator

End point title	Objective Response Rate (ORR) for Cohort 2 as Determined by the Investigator[2][3]

End point description:

ORR was defined as the percentage of participants with a complete response (CR) or partial response (PR) on two consecutive occasions ≥4 weeks apart, as determined by the investigator according to Response Evaluation Criteria in Solid Tumors, Version 1.1 (RECIST v1.1). CR was defined as the disappearance of all target lesions or any pathological lymph nodes (whether target or non-target) having a reduction in the short axis to <10 millimeters (mm). PR was defined as at least a 30% decrease in the sum of diameters of all target lesions, taking as reference the baseline sum of diameters, in the absence of CR. Participants with missing or no response assessments were classified as non-responders. ORR was calculated for each arm, along with 95% CIs using Clopper-Pearson method. Efficacy-evaluable population=all participants in Cohort 2 who received at least one dose of each drug for their assigned treatment regimen.

End point type	Primary

End point timeframe:

From randomization up to approximately 3.6 months

Notes:

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

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis for this end point.

End point values	Cohort 2: Tobemstomig + Tiragolumab			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: percentage of participants				
number (confidence interval 95%)	0 (0 to 36.94)			

Statistical analyses

No statistical analyses for this end point

Secondary: pRR for Cohort 1 as Determined by Local Pathologic Assessment

End point title	pRR for Cohort 1 as Determined by Local Pathologic

	Assessment[4]

End point description:

pRR was defined as the percentage of participants with pCR, pnCR, and pPR as determined by a local pathologic review. pCR was defined as a complete absence of viable tumor cells, pnCR as > 0 to ≤ 10% of viable tumor cells, and pPR was defined as > 10 to ≤ 50% of viable tumor cells in the dissected lymph node. Participants with missing or no pathologic response assessment, including participants who did not proceed to CLND, were classified as non-responders. pRR was calculated for each arm along with 95% CIs using Clopper-Pearson method. The difference in pRR between the experimental arms and the control arm was calculated, along with 95% CIs using the Wald method with continuity correction. Efficacy-evaluable population included all participants in Cohort 1 who received at least one dose of each drug for their assigned treatment regimen.

End point type	Secondary

End point timeframe:

Time of surgery (scheduled at Week 7)

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis for this end point.

End point values	Cohort 1: Nivolumab + Ipilimumab (Control)	Cohort 1: Tobemstomig 2100 mg	Cohort 1: Atezolizumab + Tiragolumab	Cohort 1: Tobemstomig + Tiragolumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22	40	20	20
Units: percentage of participants				
number (confidence interval 95%)	81.8 (59.72 to 94.81)	75.0 (58.80 to 87.31)	50.0 (27.20 to 72.80)	60.0 (36.05 to 80.88)

Statistical analyses

Statistical analysis title	Nivo + Ipi vs Tobe 2100 mg
Comparison groups	Cohort 1: Nivolumab + Ipilimumab (Control) v Cohort 1: Tobemstomig 2100 mg
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in pRR
Point estimate	-6.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	-31.31
upper limit	17.68

Statistical analysis title	Nivo + Ipi vs Tobe + Tira
Comparison groups	Cohort 1: Nivolumab + Ipilimumab (Control) v Cohort 1: Tobemstomig + Tiragolumab

Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in pRR
Point estimate	-21.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	-53.44
upper limit	9.8

Statistical analysis title	Nivo + Ipi vs Atezo + Tira
Comparison groups	Cohort 1: Nivolumab + Ipilimumab (Control) v Cohort 1: Atezolizumab + Tiragolumab
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in pRR
Point estimate	-31.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	-63.79
upper limit	0.16

Secondary: Event-free Survival (EFS) for Cohort 1

End point title	Event-free Survival (EFS) for Cohort 1[5]

End point description:

EFS=time from randomization to any of following events (whichever occurs first): documented disease progression (PD) that precludes surgery, as assessed by investigator per RECIST v1.1, local, regional/distant disease recurrence/death from any cause. PD=≤20% increase in smallest sum of diameter (SOD) of target lesions, taking as reference smallest SOD on study (including baseline). Local recurrence=tumor regrowth within 2cm of primary lesion's tumor bed; regional recurrence=nodal/non-nodal tumor lesions >2cm from primary lesion but not beyond regional nodal basin; distant recurrence=non-local/non-regional recurrence. Participants without disease recurrence/PD/death at the time of analysis were censored at the time of last tumor assessment. Kaplan-Meier method was used to estimate the median EFS & 95% CI constructed using Brookmeyer & Crowley method. Efficacy-evaluable population was used. 99999=median & upper limit of the 95% CI was not estimable due to insufficient number of events.

End point type	Secondary

End point timeframe:

From randomization to disease progression, disease recurrence or death or last tumor assessment (up to 22.5 months)

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis for this end point.

End point values	Cohort 1: Nivolumab + Ipilimumab (Control)	Cohort 1: Tobemstomig 2100 mg	Cohort 1: Atezolizumab + Tiragolumab	Cohort 1: Tobemstomig + Tiragolumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22	40	20	20
Units: months				
median (confidence interval 95%)	19.55 (19.55 to 99999)	99999 (14.09 to 99999)	22.51 (6.08 to 99999)	99999 (6.51 to 99999)

Statistical analyses

Statistical analysis title	Nivo + Ipi vs Tobe 2100 mg
Comparison groups	Cohort 1: Nivolumab + Ipilimumab (Control) v Cohort 1: Tobemstomig 2100 mg
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hazard ratio (HR)
Point estimate	2.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.42
upper limit	10.42

Statistical analysis title	Nivo + Ipi vs Tobe + Tira
Comparison groups	Cohort 1: Nivolumab + Ipilimumab (Control) v Cohort 1: Tobemstomig + Tiragolumab
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hazard ratio (HR)
Point estimate	6.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	53.7

Statistical analysis title	Nivo + Ipi vs Atezo + Tira
Comparison groups	Cohort 1: Nivolumab + Ipilimumab (Control) v Cohort 1: Atezolizumab + Tiragolumab

Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hazard ratio (HR)
Point estimate	3.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.79
upper limit	19.7

Secondary: Overall Survival (OS) for Cohort 1

End point title	Overall Survival (OS) for Cohort 1[6]

End point description:

OS was defined as the time from randomization to death from any cause. 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, 95% CIs were constructed using the Brookmeyer and Crowley method. Efficacy-evaluable population included all participants in Cohort 1 who received at least one dose of each drug for their assigned treatment regimen. 9999 = The median and 95% CI was not estimable due to insufficient number of participants with events.

End point type	Secondary

End point timeframe:

From randomization to death from any cause or last known to be alive (Up to 25 months)

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: No statistical analysis for this end point.

End point values	Cohort 1: Nivolumab + Ipilimumab (Control)	Cohort 1: Tobemstomig 2100 mg	Cohort 1: Atezolizumab + Tiragolumab	Cohort 1: Tobemstomig + Tiragolumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22	40	20	20
Units: months				
median (confidence interval 95%)	9999 (9999 to 9999)	9999 (9999 to 9999)	9999 (9999 to 9999)	9999 (9999 to 9999)

Statistical analyses

Statistical analysis title	Nivo + Ipi vs Tobe 2100 mg
Comparison groups	Cohort 1: Nivolumab + Ipilimumab (Control) v Cohort 1: Tobemstomig 2100 mg
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hazard ratio (HR)
Point estimate	0.78

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.05
upper limit	12.39

Statistical analysis title	Nivo + Ipi vs Tobe + Tira
Comparison groups	Cohort 1: Nivolumab + Ipilimumab (Control) v Cohort 1: Tobemstomig + Tiragolumab
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hazard ratio (HR)
Point estimate	1.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.07
upper limit	18.58

Statistical analysis title	Nivo + Ipi vs Atezo + Tira
Comparison groups	Cohort 1: Nivolumab + Ipilimumab (Control) v Cohort 1: Atezolizumab + Tiragolumab
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hazard ratio (HR)
Point estimate	2.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.23
upper limit	28.65

Secondary: Relapse-free Survival (RFS) for Cohort 1

End point title	Relapse-free Survival (RFS) for Cohort 1[7]

End point description:

RFS was defined as the time from surgery to first documented recurrence of disease/death from any cause. Recurrent disease includes local, regional/distant recurrence. Local recurrence=tumor regrowth within 2cm of primary lesion’s tumor bed; regional recurrence = any nodal/non-nodal tumor lesions that are more than 2cm from primary lesion but are not beyond the regional nodal basin; distant recurrence = any non-local/non-regional recurrence. Participants without disease recurrence or death at the time of analysis were censored at the last tumor assessment. Kaplan-Meier method was used to estimate median for RFS, and 95% CIs were constructed using Brookmeyer and Crowley method. Adjuvant evaluable population included participants in Cohort 1 who had completed surgery (CLND). 99999=The upper limit of the 95% CI was not estimable due to insufficient number of participants with events. 9999=The median and 95% CI was not estimable due to insufficient number of participants with events.

End point type	Secondary

End point timeframe:

From surgery (scheduled at Week 7) to first documented disease recurrence or death or last tumor assessment (up to 20.9 months)

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis for this end point.

End point values	Cohort 1: Nivolumab + Ipilimumab (Control)	Cohort 1: Tobemstomig 2100 mg	Cohort 1: Atezolizumab + Tiragolumab	Cohort 1: Tobemstomig + Tiragolumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22	38	18	19
Units: months				
median (confidence interval 95%)	17.91 (17.91 to 99999)	17.08 (11.79 to 99999)	20.90 (4.40 to 99999)	9999 (9999 to 9999)

Statistical analyses

Statistical analysis title	Nivo + Ipi vs Tobe 2100 mg
Comparison groups	Cohort 1: Nivolumab + Ipilimumab (Control) v Cohort 1: Tobemstomig 2100 mg
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hazard ratio (HR)
Point estimate	1.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.25
upper limit	7.75

Statistical analysis title	Nivo + Ipi vs Tobe + Tira
Comparison groups	Cohort 1: Nivolumab + Ipilimumab (Control) v Cohort 1: Tobemstomig + Tiragolumab
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hazard ratio (HR)
Point estimate	2.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.22
upper limit	26.32

Statistical analysis title	Nivo + Ipi vs Atezo + Tira
Comparison groups	Cohort 1: Nivolumab + Ipilimumab (Control) v Cohort 1: Atezolizumab + Tiragolumab
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Hazard ratio (HR)
Point estimate	2.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.35
upper limit	12.62

Secondary: ORR for Cohort 1

End point title	ORR for Cohort 1[8]

End point description:

ORR was defined as the percentage of participants with a CR or PR, as determined by the investigator according to RECIST v1.1. CR was defined as the disappearance of all target lesions or any pathological lymph nodes (whether target or non-target) having a reduction in short axis to <10 mm. PR was defined as at least a 30% decrease in the sum of diameters of all target lesions, taking as reference the baseline sum of diameters, in the absence of CR. Participants with missing or no response assessments were classified as non-responders. ORR was calculated for each arm, along with 95% CIs using the Clopper-Pearson method. The difference in ORR between the experimental arms and the control arm was calculated, along with 95% CIs using the Wald method with continuity correction. Efficacy-evaluable population included all participants in Cohort 1 who received at least one dose of each drug for their assigned treatment regimen.

End point type	Secondary

End point timeframe:

Prior to surgery (up to Week 6)

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis for this end point.

End point values	Cohort 1: Nivolumab + Ipilimumab (Control)	Cohort 1: Tobemstomig 2100 mg	Cohort 1: Atezolizumab + Tiragolumab	Cohort 1: Tobemstomig + Tiragolumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22	40	20	20
Units: percentage of participants				
number (confidence interval 95%)	59.1 (36.35 to 79.29)	37.5 (22.73 to 54.20)	35.0 (15.39 to 59.22)	60.0 (36.05 to 80.88)

Statistical analyses

Statistical analysis title	Nivo + Ipi vs Tobe 2100 mg
Comparison groups	Cohort 1: Nivolumab + Ipilimumab (Control) v Cohort 1: Tobemstomig 2100 mg
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in ORR
Point estimate	-21.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	-50.55
upper limit	7.37

Statistical analysis title	Nivo + Ipi vs Tobe + Tira
Comparison groups	Cohort 1: Nivolumab + Ipilimumab (Control) v Cohort 1: Tobemstomig + Tiragolumab
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in ORR
Point estimate	0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	-33.58
upper limit	35.4

Statistical analysis title	Nivo + Ipi vs Atezo + Tira
Comparison groups	Cohort 1: Atezolizumab + Tiragolumab v Cohort 1: Nivolumab + Ipilimumab (Control)
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in ORR
Point estimate	-24.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-58.17
upper limit	9.99

Secondary: Number of Participants with Adverse Events (AEs) and Severity of AEs Determined According to National Cancer Institute Common Terminology Criteria for Adverse Events, Version 5.0 (NCI CTCAE v5.0) for Cohort 1

End point title	Number of Participants with Adverse Events (AEs) and Severity of AEs Determined According to National Cancer Institute Common Terminology Criteria for Adverse Events, Version 5.0 (NCI CTCAE v5.0) for Cohort 1[9]

End point description:

An AE=any untoward medical occurrence in clinical investigation participant administered a pharmaceutical product, regardless of causal attribution. AE can therefore be any unfavorable & unintended sign, symptom/disease temporally associated with using an investigational product, whether or not considered related to the investigational product. Severity was determined per NCI CTCAE v5.0 Grade 1: Mild; asymptomatic/mild symptoms; clinical/diagnostic observations only; or intervention not indicated; Grade 2: Moderate; minimal, local/non-invasive intervention indicated; or limiting age-appropriate instrumental activities of daily living (ADL); Grade 3: Severe/medically significant, but not immediately life-threatening: hospitalization/prolongation of hospitalization indicated; disabling/limiting self-care ADL; Grade 4: Life-threatening consequences/urgent intervention indicated; Grade 5: Death related to AE. Multiple occurrences of AEs in 1 individual are counted once at highest grade.

End point type	Secondary

End point timeframe:

From initiation of study treatment up to 135 days after the final dose of study treatment (Up to 5.6 months)

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: No statistical analysis for this end point.

End point values	Cohort 1: Nivolumab + Ipilimumab (Control)	Cohort 1: Tobemstomig 2100 mg	Cohort 1: Atezolizumab + Tiragolumab	Cohort 1: Tobemstomig + Tiragolumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22	40	20	20
Units: participants				
AE, Any Grade	19	36	19	18
Worst Grade, Grade 1 AE	4	13	9	4
Worst Grade, Grade 2 AE	9	15	9	8
Worst Grade, Grade 3 AE	4	5	1	6
Worst Grade, Grade 4 AE	2	3	0	0
Worst Grade, Grade 5 AE	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Immune-related AEs Grade ≥ 3 for Cohort 1

End point title	Number of Participants With Immune-related AEs Grade ≥ 3 for Cohort 1[10]

End point description:

An AE was any untoward medical occurrence in a clinical investigation participant administered a pharmaceutical product, regardless of causal attribution. An AE can therefore be any unfavorable & unintended sign (including an abnormal laboratory finding), symptom/disease temporally associated with the use of an investigational product, whether or not considered related to the investigational product. Participants with immune-related adverse events Grade ≥ 3 were reported. Safety-evaluable population included all randomized participants in Cohort 1 who received any amount of the study treatment.

End point type	Secondary

End point timeframe:

From initiation of study treatment up to 135 days after the final dose of study treatment (Up to 5.6

months)

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis for this end point.

End point values	Cohort 1: Nivolumab + Ipilimumab (Control)	Cohort 1: Tobemstomig 2100 mg	Cohort 1: Atezolizumab + Tiragolumab	Cohort 1: Tobemstomig + Tiragolumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22	40	20	20
Units: participants	15	29	8	13

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Surgery Delay due to Treatment-related AEs

End point title	Duration of Surgery Delay due to Treatment-related AEs[11]

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 more than 2 weeks. An AE was any untoward medical occurrence in a clinical investigation participants administered a pharmaceutical product, regardless of causal attribution. An AE can therefore be any unfavorable & unintended sign (including an abnormal laboratory finding), symptom/disease temporally associated with the use of the investigational product, whether considered related to the investigational product. Safety-evaluable population included all randomized participants in Cohort 1 who received any amount of the study treatment. Participants with a surgery delay of more than 2 weeks due to treatment-related AE were analyzed. 9999=Standard Deviation (SD) was not estimable due to insufficient number of participants with events.

End point type	Secondary

End point timeframe:

Time of surgery (scheduled at Week 7)

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis for this end point.

End point values	Cohort 1: Nivolumab + Ipilimumab (Control)	Cohort 1: Tobemstomig 2100 mg	Cohort 1: Atezolizumab + Tiragolumab	Cohort 1: Tobemstomig + Tiragolumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	1	0[12]	1
Units: weeks				
arithmetic mean (standard deviation)	17.0 (± 14.8)	5.1 (± 9999)	()	3.0 (± 9999)

Notes:

[12] - No participants had a delay in surgery.

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[13]

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 more than 2 weeks. An AE was any untoward medical occurrence in a clinical investigation participants administered a pharmaceutical product, regardless of causal attribution. An AE can therefore be any unfavorable & unintended sign (including an abnormal laboratory finding), symptom/disease temporally associated with the use of the investigational product, whether considered related to the investigational product. Safety-evaluable population included all randomized participants in Cohort 1 who received any amount of the study treatment.

End point type	Secondary

End point timeframe:

Time of surgery (scheduled at Week 7)

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis for this end point.

End point values	Cohort 1: Nivolumab + Ipilimumab (Control)	Cohort 1: Tobemstomig 2100 mg	Cohort 1: Atezolizumab + Tiragolumab	Cohort 1: Tobemstomig + Tiragolumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22	40	20	20
Units: percentage of participants				
number (not applicable)	13.6	5.0	0	5.0

Statistical analyses

No statistical analyses for this end point

Secondary: Surgical Complication Rates for Cohort 1

End point title	Surgical Complication Rates for Cohort 1[14]

End point description:

Surgical complications were scored per Clavien-Dindo surgical classification. Complication rates for every grade were reported & scored for participants who underwent CLND. Surgical complications per Clavien-Dindo are classified as: 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 requiring surgical, endoscopic/radiological intervention with (Grade IIIb)/without (Grade IIIa) general anesthesia. Grade IV=Life-threatening complications requiring intensive care unit (ICU) management, can be single organ (Grade IVa)/multiorgan (Grade IVb) dysfunction. Grade V=Complications that might cause death of participant. Safety-evaluable population. Number analyzed=number of participants who underwent CLND. n=number of participants with surgical complication. TDV=Treatment discontinuation visit.

End point type	Secondary

End point timeframe:

At treatment discontinuation visit (Week 13) and Surgery Follow-Up (6 months after surgery)

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analysis for this end point.

End point values	Cohort 1: Nivolumab + Ipilimumab (Control)	Cohort 1: Tobemstomig 2100 mg	Cohort 1: Atezolizumab + Tiragolumab	Cohort 1: Tobemstomig + Tiragolumab
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	22	38	18	19
Units: percentage of participants				
number (not applicable)				
TDV: Grade 0 (n=22,38,18,19)	0	0	5.55	54.26
TDV: Grade I (n=22,38,18,19)	18.18	5.26	22.22	0
TDV: Grade II (n=22,38,18,19)	13.63	18.42	16.66	10.52
TDV: Grade IIIa (n=22,38,18,19)	0	7.89	0	54.26
TDV: Grade IIIb (n=22,38,18,19)	0	2.63	0	10.52
TDV: Grade IVa (n=22,38,18,19)	0	2.63	0	0
Follow-up Month 6: Grade 0 (n=22,37,17,17)	0	0	5.88	0
Follow-up Month 6: Grade I (n=22,37,17,17)	13.63	8.10	17.64	0
Follow-up Month 6: Grade II (n=22,37,17,17)	4.540	10.81	5.88	0
Follow-up Month 6: Grade IIIa (n=22,37,17,17)	0	13.51	5.88	0
Follow-up Month 6: Grade IIIb (n=22,37,17,17)	0	0	0	11.76
Follow-up Month 6: Grade IVa (n=22,37,17,17)	0	2.7	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR) for Cohort 2

End point title	Duration of Response (DOR) for Cohort 2[15]

End point description:

DOR=time from first occurrence of a documented objective response (OR) to PD/death from any cause (whichever occurred first), as determined by the investigator according to RECIST v1.1. OR was defined as a CR or PR on two consecutive occasions ≥ 4 weeks apart, as determined by the investigator according to RECIST v1.1. CR = disappearance of all target lesions or any pathological lymph nodes (whether target or non-target) having a reduction in short axis to <10 mm. PR = at least a 30% decrease in the SOD of all target lesions, taking as reference the baseline SOD, in the absence of CR. PD was defined as at least a 20% increase in the SOD of target lesions, taking as reference the smallest SOD on the study (including baseline). Participants without PD or death at time of analysis were censored at time of last tumor assessment. Kaplan-Meier method was used to estimate median for DOR, with 95% CIs constructed using Brookmeyer & Crowley method. Efficacy-evaluable population.

End point type	Secondary

End point timeframe:

Time from the first occurrence of a documented OR to PD or death from any cause (up to 3.6 months)

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analysis for this end point.

End point values	Cohort 2: Tobemstomig + Tiragolumab			
Subject group type	Reporting group			
Number of subjects analysed	0[16]			
Units: months				
median (confidence interval 95%)	(to)			

Notes:

[16] - DOR was only evaluated in participants who achieved an OR (CR or PR).

Statistical analyses

No statistical analyses for this end point

Secondary: OS Rates at Specific Timepoints for Cohort 2

End point title	OS Rates at Specific Timepoints for Cohort 2[17]

End point description:

OS was defined as the time from randomization to death from any cause. OS rate is percentage of participants who were event free for OS. Participants who were still alive at the time of OS analysis were censored at the last date they were known to be alive. OS rate at specific time points were estimated using the Kaplan-Meier method, with 95% CIs calculated based on Greenwood's estimate for the variance. Efficacy-evaluable population included all participants in Cohort 2 who received at least one dose of each drug for their assigned treatment regimen. 'n' for each 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.

End point type	Secondary

End point timeframe:

Months 3, 6 and 12

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: No statistical analysis for this end point.

End point values	Cohort 2: Tobemstomig + Tiragolumab			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: percentage of participants				
number (confidence interval 95%)				
3 months (n=7)	100.0 (100.0 to 100.0)			
6 months (n=4)	71.43 (37.96 to 100.0)			
12 months (n=2)	47.62 (3.47 to 91.77)			

Statistical analyses

No statistical analyses for this end point

Secondary: OS for Cohort 2

End point title	OS for Cohort 2[18]

End point description:

OS was defined as the time from randomization to death from any cause. 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, with 95% CIs constructed by using the Brookmeyer and Crowley method. Efficacy-evaluable population included all participants in Cohort 2 who received at least one dose of each drug for their assigned treatment regimen. 99999 = The upper limit of the 95% CI was not estimable due to insufficient number of participants with events.

End point type	Secondary

End point timeframe:

From randomization/enrollment to death from any cause or last known to be alive (Up to 24.2 months)

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis for this end point.

End point values	Cohort 2: Tobemstomig + Tiragolumab			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: months				
median (confidence interval 95%)	8.94 (4.17 to 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival (PFS) for Cohort 2

End point title	Progression-Free Survival (PFS) for Cohort 2[19]

End point description:

PFS after randomization/enrollment was defined as the time from randomization/enrollment to the first occurrence of PD or death from any cause (whichever occurred first), as determined by the investigator according to RECIST v1.1. PD was defined as at least a 20% increase in the SOD of target lesions, taking as reference the smallest SOD on the study (including baseline) and/or unequivocal progression of a non-target lesion and/or any new lesion. Participants without documented PD or death at the time of analysis were censored at the day of the last tumor assessment. Kaplan-Meier method was used to estimate the median for PFS, with 95% CIs constructed by using the Brookmeyer and Crowley method. Efficacy-evaluable population included all participants in Cohort 2 who received at least one dose of each drug for their assigned treatment regimen.

End point type	Secondary

End point timeframe:

From randomization/enrollment to first documented disease progression or death or last tumor assessment (up to 3.6 months)

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis for this end point.

End point values	Cohort 2: Tobemstomig + Tiragolumab			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: months				
median (confidence interval 95%)	2.07 (1.68 to 2.37)			

Statistical analyses

No statistical analyses for this end point

Secondary: Disease Control Rate (DCR) for Cohort 2

End point title	Disease Control Rate (DCR) for Cohort 2[20]

End point description:

DCR was defined as the percentage of participants with stable disease for ≥ 12 weeks or a CR or PR, as determined by the investigator according to RECIST v1.1. CR was defined as the disappearance of all target lesions. PR was defined as at least a 30% decrease in the sum of diameters of all target lesions, taking as reference the baseline sum of diameters, in the absence of CR. Stable disease was defined as neither sufficient shrinkage to qualify for CR or PR nor sufficient increase to qualify for PD. PD was defined as at least a 20% increase in the SOD of target lesions, taking as reference the smallest SOD on the study (including baseline). DCR was calculated for each treatment arm, with 95% CIs estimated through use of Clopper-Pearson's exact method. Efficacy-evaluable population included all participants in Cohort 2 who received at least one dose of each drug for their assigned treatment regimen.

End point type	Secondary

End point timeframe:

From randomization up to 3.6 months

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis for this end point.

End point values	Cohort 2: Tobemstomig + Tiragolumab			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: percentage of participants				
number (confidence interval 95%)	0 (0.00 to 36.94)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With AEs and Severity of AEs Determined According to NCI CTCAE v5.0 for Cohort 2

End point title	Number of Participants With AEs and Severity of AEs Determined According to NCI CTCAE v5.0 for Cohort 2[21]

End point description:

AE=untoward medical occurrence in participant administered a drug, regardless of causal attribution.AE can be any unfavorable & unintended sign (abnormal laboratory), symptom/disease temporally associated with use of drug, whether/not considered related to drug. Severity of AEs per NCI CTCAE v5.0 Grade 1:Mild;asymptomatic/mild symptoms;clinical/diagnostic observations only;or intervention not indicated;Grade 2:Moderate;minimal, local/non-invasive intervention indicated/limiting age-appropriate instrumental activities of daily living; Grade 3: Severe/medically significant,but not immediately life-threatening:hospitalization/prolongation of hospitalization indicated;disabling/limiting self-care activities of daily living; Grade 4:Life-threatening consequences/urgent intervention indicated; Grade 5:Death related to AE. Safety-evaluable population. AEs were reported until 30 days after final dose/until initiation of new systemic anti-cancer therapy (whichever occurs first).

End point type	Secondary

End point timeframe:

From initiation of study treatment up to 135 days after the final dose of study treatment (Up to 10 months)

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis for this end point.

End point values	Cohort 2: Tobemstomig + Tiragolumab			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: participants				
AE, Any Grade	7			
Worst Grade, Grade 1 AE	0			
Worst Grade, Grade 2 AE	6			
Worst Grade, Grade 3 AE	1			
Worst Grade, Grade 4 AE	0			
Worst Grade, Grade 5 AE	0			

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

AEs: From initiation of study treatment up to 135 days after final dose (Cohort 1: Up to 5.6 months; Cohort 2: 10 months); All-cause Mortality: Randomization up to end of long-term follow-up (Cohort 1: Up to approximately 25 months; Cohort 2: 24.2 months)

Adverse event reporting additional description:

Safety evaluable population included all randomized participants who received at least one dose of the study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.0

Reporting groups

Reporting group title	Cohort 1: Nivolumab + Ipilimumab (Control)

Reporting group description:

Participants received nivolumab 3 mg/kg IV and ipilimumab 1 mg/kg IV on Day 1 of each 21-day cycle for 2 cycles (6 weeks) until surgery (Week 7) or until unacceptable toxicity or loss of clinical benefit, whichever occurs first. Post-surgery at the discretion of the investigator, participants started either adjuvant therapy or an observation phase from Week 13.

Reporting group title	Cohort 1: Tobemstomig 2100 mg

Reporting group description:

Participants received a fixed dose of tobemstomig 2100 mg IV on Day 1 of each 21-day cycle for 2 cycles (6 weeks) until surgery (Week 7) or until unacceptable toxicity or loss of clinical benefit, whichever occurs first. Post-surgery at the discretion of the investigator, participants started either adjuvant therapy or an observation phase from Week 13.

Reporting group title	Cohort 2: Tobemstomig + Tiragolumab

Reporting group description:

Participants received tobemstomig 2100 mg IV and tiragolumab 600 mg IV on Day 1 of each 21-day cycle until unacceptable toxicity or loss of clinical benefit as determined by the investigator after an integrated assessment of radiographic and biochemical data, local biopsy results (if available), and clinical status.

Reporting group title	Cohort 1: Tobemstomig + Tiragolumab

Reporting group description:

Participants received tobemstomig 2100 mg IV and tiragolumab 600 mg IV on Day 1 of each 21-day cycle for 2 cycles (6 weeks) until surgery (Week 7) or until unacceptable toxicity or loss of clinical benefit, whichever occurs first. Post-surgery at the discretion of the investigator, participants started either adjuvant therapy or an observation phase from Week 13.

Reporting group title	Cohort 1: Atezolizumab + Tiragolumab

Reporting group description:

Participants received atezolizumab 1200 mg IV and tiragolumab 600 mg IV on Day 1 of each 21-day cycle for 2 cycles (6 weeks) until surgery (Week 7) or until unacceptable toxicity or loss of clinical benefit, whichever occurs first. Post-surgery at the discretion of the investigator, participants started either adjuvant therapy or an observation phase from Week 13.

Serious adverse events	Cohort 1: Nivolumab + Ipilimumab (Control)	Cohort 1: Tobemstomig 2100 mg	Cohort 2: Tobemstomig + Tiragolumab
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 22 (18.18%)	9 / 40 (22.50%)	1 / 8 (12.50%)
number of deaths (all causes)	1	1	5
number of deaths resulting from	0	0	0

adverse events			
Investigations			
Troponin increased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 40 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Heart rate irregular			
subjects affected / exposed	1 / 22 (4.55%)	0 / 40 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	0 / 22 (0.00%)	0 / 40 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound dehiscence			
subjects affected / exposed	1 / 22 (4.55%)	1 / 40 (2.50%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haematoma			
subjects affected / exposed	0 / 22 (0.00%)	1 / 40 (2.50%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 22 (0.00%)	1 / 40 (2.50%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematoma			
subjects affected / exposed	0 / 22 (0.00%)	0 / 40 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphatic fistula			

subjects affected / exposed	0 / 22 (0.00%)	0 / 40 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Ventricular fibrillation			
subjects affected / exposed	0 / 22 (0.00%)	1 / 40 (2.50%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocarditis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 40 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial ischaemia			
subjects affected / exposed	0 / 22 (0.00%)	1 / 40 (2.50%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Scar excision			
subjects affected / exposed	1 / 22 (4.55%)	0 / 40 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	0 / 22 (0.00%)	1 / 40 (2.50%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enteritis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 40 (0.00%)	1 / 8 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Immune-mediated hepatitis			

subjects affected / exposed	1 / 22 (4.55%)	0 / 40 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pneumonitis			
subjects affected / exposed	1 / 22 (4.55%)	0 / 40 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune-mediated lung disease			
subjects affected / exposed	1 / 22 (4.55%)	0 / 40 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Myositis			
subjects affected / exposed	0 / 22 (0.00%)	1 / 40 (2.50%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Catheter site infection			
subjects affected / exposed	0 / 22 (0.00%)	1 / 40 (2.50%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	1 / 22 (4.55%)	1 / 40 (2.50%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative wound infection			
subjects affected / exposed	0 / 22 (0.00%)	0 / 40 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			

subjects affected / exposed	0 / 22 (0.00%)	1 / 40 (2.50%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis aseptic			
subjects affected / exposed	1 / 22 (4.55%)	0 / 40 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infected seroma			
subjects affected / exposed	0 / 22 (0.00%)	1 / 40 (2.50%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Diabetic ketoacidosis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 40 (0.00%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperlipasaemia			
subjects affected / exposed	0 / 22 (0.00%)	1 / 40 (2.50%)	0 / 8 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Cohort 1: Tobemstomig + Tiragolumab	Cohort 1: Atezolizumab + Tiragolumab	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 20 (30.00%)	3 / 20 (15.00%)	
number of deaths (all causes)	1	2	
number of deaths resulting from adverse events	0	0	
Investigations			
Troponin increased			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Heart rate irregular			

subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound dehiscence			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haematoma			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphatic fistula			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Ventricular fibrillation			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Myocarditis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial ischaemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Scar excision			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Immune-mediated hepatitis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pneumonitis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune-mediated lung disease			

subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Myositis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Catheter site infection			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound infection			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis aseptic			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected seroma			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Metabolism and nutrition disorders			
Diabetic ketoacidosis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperlipasaemia			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 0	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	Cohort 1: Nivolumab + Ipilimumab (Control)	Cohort 1: Tobemstomig 2100 mg	Cohort 2: Tobemstomig + Tiragolumab
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 22 (81.82%)	34 / 40 (85.00%)	7 / 8 (87.50%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 22 (0.00%)	0 / 40 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 22 (0.00%)	0 / 40 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Lymphoedema			
subjects affected / exposed	1 / 22 (4.55%)	0 / 40 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 22 (9.09%)	2 / 40 (5.00%)	0 / 8 (0.00%)
occurrences (all)	2	2	0
Chest pain			
subjects affected / exposed	1 / 22 (4.55%)	0 / 40 (0.00%)	1 / 8 (12.50%)
occurrences (all)	1	0	1
Hyperthermia			

subjects affected / exposed	0 / 22 (0.00%)	0 / 40 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	7 / 22 (31.82%)	15 / 40 (37.50%)	4 / 8 (50.00%)
occurrences (all)	7	15	4
Extravasation			
subjects affected / exposed	0 / 22 (0.00%)	0 / 40 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 22 (0.00%)	1 / 40 (2.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Influenza like illness			
subjects affected / exposed	1 / 22 (4.55%)	1 / 40 (2.50%)	1 / 8 (12.50%)
occurrences (all)	1	1	1
Pain			
subjects affected / exposed	0 / 22 (0.00%)	1 / 40 (2.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Peripheral swelling			
subjects affected / exposed	0 / 22 (0.00%)	0 / 40 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Pyrexia			
subjects affected / exposed	1 / 22 (4.55%)	0 / 40 (0.00%)	2 / 8 (25.00%)
occurrences (all)	1	0	4
Xerosis			
subjects affected / exposed	2 / 22 (9.09%)	0 / 40 (0.00%)	0 / 8 (0.00%)
occurrences (all)	2	0	0
Oedema peripheral			
subjects affected / exposed	0 / 22 (0.00%)	2 / 40 (5.00%)	1 / 8 (12.50%)
occurrences (all)	0	2	2
Immune system disorders			
Contrast media allergy			
subjects affected / exposed	2 / 22 (9.09%)	0 / 40 (0.00%)	0 / 8 (0.00%)
occurrences (all)	2	0	0
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	2 / 22 (9.09%)	2 / 40 (5.00%)	2 / 8 (25.00%)
occurrences (all)	2	2	2
Dyspnoea			
subjects affected / exposed	2 / 22 (9.09%)	1 / 40 (2.50%)	0 / 8 (0.00%)
occurrences (all)	2	1	0
Haemoptysis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 40 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	2
Oropharyngeal pain			
subjects affected / exposed	0 / 22 (0.00%)	1 / 40 (2.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Pleural effusion			
subjects affected / exposed	0 / 22 (0.00%)	0 / 40 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 22 (0.00%)	0 / 40 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	1 / 22 (4.55%)	1 / 40 (2.50%)	0 / 8 (0.00%)
occurrences (all)	1	1	0
Sleep disorder			
subjects affected / exposed	0 / 22 (0.00%)	0 / 40 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	3 / 22 (13.64%)	2 / 40 (5.00%)	0 / 8 (0.00%)
occurrences (all)	3	2	0
Amylase increased			
subjects affected / exposed	0 / 22 (0.00%)	3 / 40 (7.50%)	0 / 8 (0.00%)
occurrences (all)	0	3	0
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 22 (4.55%)	2 / 40 (5.00%)	0 / 8 (0.00%)
occurrences (all)	1	2	0
Blood creatinine increased			

subjects affected / exposed	1 / 22 (4.55%)	2 / 40 (5.00%)	0 / 8 (0.00%)
occurrences (all)	1	2	0
International normalised ratio decreased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 40 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Lipase increased			
subjects affected / exposed	2 / 22 (9.09%)	3 / 40 (7.50%)	1 / 8 (12.50%)
occurrences (all)	2	4	1
SARS-CoV-2 test positive			
subjects affected / exposed	0 / 22 (0.00%)	1 / 40 (2.50%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Serum ferritin decreased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 40 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Troponin increased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 40 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 22 (0.00%)	0 / 40 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Procedural nausea			
subjects affected / exposed	0 / 22 (0.00%)	2 / 40 (5.00%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
Post procedural constipation			
subjects affected / exposed	0 / 22 (0.00%)	1 / 40 (2.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Joint injury			
subjects affected / exposed	0 / 22 (0.00%)	0 / 40 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Infusion related reaction			
subjects affected / exposed	2 / 22 (9.09%)	6 / 40 (15.00%)	0 / 8 (0.00%)
occurrences (all)	2	8	0
Procedural pain			

subjects affected / exposed	2 / 22 (9.09%)	8 / 40 (20.00%)	0 / 8 (0.00%)
occurrences (all)	2	8	0
Seroma			
subjects affected / exposed	0 / 22 (0.00%)	1 / 40 (2.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Skin laceration			
subjects affected / exposed	0 / 22 (0.00%)	0 / 40 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Cardiac disorders			
Sinus bradycardia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 40 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 22 (9.09%)	1 / 40 (2.50%)	0 / 8 (0.00%)
occurrences (all)	2	1	0
Dysgeusia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 40 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	2 / 22 (9.09%)	1 / 40 (2.50%)	2 / 8 (25.00%)
occurrences (all)	2	1	2
Hypoaesthesia			
subjects affected / exposed	2 / 22 (9.09%)	1 / 40 (2.50%)	0 / 8 (0.00%)
occurrences (all)	2	1	0
Lethargy			
subjects affected / exposed	0 / 22 (0.00%)	0 / 40 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Paraesthesia			
subjects affected / exposed	1 / 22 (4.55%)	0 / 40 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Sensory disturbance			
subjects affected / exposed	0 / 22 (0.00%)	0 / 40 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			

Thrombocytopenia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 40 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Lymphadenopathy			
subjects affected / exposed	0 / 22 (0.00%)	0 / 40 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Anaemia			
subjects affected / exposed	1 / 22 (4.55%)	2 / 40 (5.00%)	2 / 8 (25.00%)
occurrences (all)	1	2	3
Eye disorders			
Retinal detachment			
subjects affected / exposed	0 / 22 (0.00%)	0 / 40 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Eyelid ptosis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 40 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Dry eye			
subjects affected / exposed	0 / 22 (0.00%)	2 / 40 (5.00%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
Gastrointestinal disorders			
Gastrointestinal pain			
subjects affected / exposed	0 / 22 (0.00%)	0 / 40 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	4 / 22 (18.18%)	1 / 40 (2.50%)	1 / 8 (12.50%)
occurrences (all)	4	1	1
Vomiting			
subjects affected / exposed	1 / 22 (4.55%)	0 / 40 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Dry mouth			
subjects affected / exposed	2 / 22 (9.09%)	3 / 40 (7.50%)	0 / 8 (0.00%)
occurrences (all)	2	3	0
Diarrhoea			
subjects affected / exposed	2 / 22 (9.09%)	3 / 40 (7.50%)	3 / 8 (37.50%)
occurrences (all)	2	3	3
Constipation			

subjects affected / exposed	2 / 22 (9.09%)	3 / 40 (7.50%)	1 / 8 (12.50%)
occurrences (all)	2	3	1
Abdominal tenderness			
subjects affected / exposed	0 / 22 (0.00%)	0 / 40 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Abdominal pain			
subjects affected / exposed	1 / 22 (4.55%)	1 / 40 (2.50%)	2 / 8 (25.00%)
occurrences (all)	2	1	3
Hepatobiliary disorders			
Hepatitis			
subjects affected / exposed	2 / 22 (9.09%)	2 / 40 (5.00%)	0 / 8 (0.00%)
occurrences (all)	2	2	0
Hypertransaminasaemia			
subjects affected / exposed	1 / 22 (4.55%)	2 / 40 (5.00%)	0 / 8 (0.00%)
occurrences (all)	1	2	0
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	1 / 22 (4.55%)	3 / 40 (7.50%)	0 / 8 (0.00%)
occurrences (all)	1	3	0
Dry skin			
subjects affected / exposed	0 / 22 (0.00%)	1 / 40 (2.50%)	1 / 8 (12.50%)
occurrences (all)	0	1	1
Eczema			
subjects affected / exposed	1 / 22 (4.55%)	0 / 40 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 40 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Lichenoid keratosis			
subjects affected / exposed	2 / 22 (9.09%)	2 / 40 (5.00%)	0 / 8 (0.00%)
occurrences (all)	3	4	0
Pruritus			
subjects affected / exposed	8 / 22 (36.36%)	6 / 40 (15.00%)	2 / 8 (25.00%)
occurrences (all)	8	6	3
Psoriasis			

subjects affected / exposed	0 / 22 (0.00%)	0 / 40 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	6 / 22 (27.27%)	7 / 40 (17.50%)	2 / 8 (25.00%)
occurrences (all)	7	8	2
Rash erythematous			
subjects affected / exposed	0 / 22 (0.00%)	0 / 40 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Renal impairment			
subjects affected / exposed	0 / 22 (0.00%)	0 / 40 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Endocrine disorders			
Thyroiditis			
subjects affected / exposed	1 / 22 (4.55%)	2 / 40 (5.00%)	0 / 8 (0.00%)
occurrences (all)	1	2	0
Hypothyroidism			
subjects affected / exposed	0 / 22 (0.00%)	3 / 40 (7.50%)	0 / 8 (0.00%)
occurrences (all)	0	3	0
Hypophysitis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 40 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Hyperthyroidism			
subjects affected / exposed	4 / 22 (18.18%)	7 / 40 (17.50%)	1 / 8 (12.50%)
occurrences (all)	4	7	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 22 (13.64%)	2 / 40 (5.00%)	0 / 8 (0.00%)
occurrences (all)	3	3	0
Joint stiffness			
subjects affected / exposed	0 / 22 (0.00%)	0 / 40 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 22 (0.00%)	0 / 40 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal stiffness			

subjects affected / exposed	0 / 22 (0.00%)	1 / 40 (2.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Myalgia			
subjects affected / exposed	1 / 22 (4.55%)	1 / 40 (2.50%)	0 / 8 (0.00%)
occurrences (all)	1	1	0
Myositis			
subjects affected / exposed	1 / 22 (4.55%)	0 / 40 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Pain in extremity			
subjects affected / exposed	0 / 22 (0.00%)	1 / 40 (2.50%)	1 / 8 (12.50%)
occurrences (all)	0	2	1
Groin pain			
subjects affected / exposed	0 / 22 (0.00%)	0 / 40 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 22 (4.55%)	0 / 40 (0.00%)	2 / 8 (25.00%)
occurrences (all)	1	0	2
Cystitis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 40 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Device related infection			
subjects affected / exposed	0 / 22 (0.00%)	0 / 40 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 22 (0.00%)	0 / 40 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 22 (0.00%)	2 / 40 (5.00%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
Hyperamylasaemia			
subjects affected / exposed	0 / 22 (0.00%)	0 / 40 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Hyperkalaemia			

subjects affected / exposed	0 / 22 (0.00%)	0 / 40 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Cohort 1: Tobemstomig + Tiragolumab	Cohort 1: Atezolizumab + Tiragolumab	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 20 (90.00%)	18 / 20 (90.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	3	0	
Vascular disorders			
Haematoma			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Lymphoedema			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 20 (5.00%)	4 / 20 (20.00%)	
occurrences (all)	1	4	
Chest pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	
occurrences (all)	0	0	
Hyperthermia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Fatigue			
subjects affected / exposed	6 / 20 (30.00%)	3 / 20 (15.00%)	
occurrences (all)	6	4	
Extravasation			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Chills			

subjects affected / exposed	4 / 20 (20.00%)	0 / 20 (0.00%)	
occurrences (all)	4	0	
Influenza like illness			
subjects affected / exposed	1 / 20 (5.00%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Pain			
subjects affected / exposed	2 / 20 (10.00%)	0 / 20 (0.00%)	
occurrences (all)	2	0	
Peripheral swelling			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	
occurrences (all)	0	0	
Pyrexia			
subjects affected / exposed	1 / 20 (5.00%)	2 / 20 (10.00%)	
occurrences (all)	1	2	
Xerosis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	
occurrences (all)	0	0	
Oedema peripheral			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Immune system disorders			
Contrast media allergy			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 20 (10.00%)	0 / 20 (0.00%)	
occurrences (all)	2	0	
Dyspnoea			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	
occurrences (all)	0	0	
Haemoptysis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	
occurrences (all)	0	0	
Oropharyngeal pain			

subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Pleural effusion			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Confusional state			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Insomnia			
subjects affected / exposed	0 / 20 (0.00%)	2 / 20 (10.00%)	
occurrences (all)	0	2	
Sleep disorder			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Amylase increased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Blood creatinine increased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	
occurrences (all)	0	0	
International normalised ratio decreased			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Lipase increased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
SARS-CoV-2 test positive			

subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	
occurrences (all)	0	0	
Serum ferritin decreased			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	
occurrences (all)	0	0	
Troponin increased			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Weight decreased			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Procedural nausea			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Post procedural constipation			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Joint injury			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Infusion related reaction			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Procedural pain			
subjects affected / exposed	3 / 20 (15.00%)	4 / 20 (20.00%)	
occurrences (all)	3	4	
Seroma			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Skin laceration			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	
occurrences (all)	0	0	
Cardiac disorders			

Sinus bradycardia subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	1 / 20 (5.00%) 1	
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	1 / 20 (5.00%) 1	
Dysgeusia subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	0 / 20 (0.00%) 0	
Headache subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 2	0 / 20 (0.00%) 0	
Hypoaesthesia subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 20 (0.00%) 0	
Lethargy subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 20 (0.00%) 0	
Paraesthesia subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	0 / 20 (0.00%) 0	
Sensory disturbance subjects affected / exposed occurrences (all)	1 / 20 (5.00%) 1	0 / 20 (0.00%) 0	
Blood and lymphatic system disorders Thrombocytopenia subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	1 / 20 (5.00%) 1	
Lymphadenopathy subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	1 / 20 (5.00%) 1	
Anaemia subjects affected / exposed occurrences (all)	0 / 20 (0.00%) 0	0 / 20 (0.00%) 0	
Eye disorders			

Retinal detachment			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Eyelid ptosis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Dry eye			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Gastrointestinal pain			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Nausea			
subjects affected / exposed	3 / 20 (15.00%)	1 / 20 (5.00%)	
occurrences (all)	3	1	
Vomiting			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Dry mouth			
subjects affected / exposed	4 / 20 (20.00%)	1 / 20 (5.00%)	
occurrences (all)	4	1	
Diarrhoea			
subjects affected / exposed	3 / 20 (15.00%)	1 / 20 (5.00%)	
occurrences (all)	5	1	
Constipation			
subjects affected / exposed	2 / 20 (10.00%)	1 / 20 (5.00%)	
occurrences (all)	2	1	
Abdominal tenderness			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	
occurrences (all)	0	0	
Abdominal pain			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	
occurrences (all)	0	0	
Hepatobiliary disorders			

Hepatitis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Hypertransaminasaemia			
subjects affected / exposed	2 / 20 (10.00%)	0 / 20 (0.00%)	
occurrences (all)	2	0	
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	2 / 20 (10.00%)	2 / 20 (10.00%)	
occurrences (all)	2	2	
Dry skin			
subjects affected / exposed	2 / 20 (10.00%)	0 / 20 (0.00%)	
occurrences (all)	2	0	
Eczema			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Hyperhidrosis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	
occurrences (all)	0	0	
Lichenoid keratosis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Pruritus			
subjects affected / exposed	5 / 20 (25.00%)	2 / 20 (10.00%)	
occurrences (all)	5	2	
Psoriasis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Rash			
subjects affected / exposed	3 / 20 (15.00%)	1 / 20 (5.00%)	
occurrences (all)	3	1	
Rash erythematous			
subjects affected / exposed	1 / 20 (5.00%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Renal and urinary disorders			

Renal impairment			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Endocrine disorders			
Thyroiditis			
subjects affected / exposed	0 / 20 (0.00%)	0 / 20 (0.00%)	
occurrences (all)	0	0	
Hypothyroidism			
subjects affected / exposed	1 / 20 (5.00%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Hypophysitis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Hyperthyroidism			
subjects affected / exposed	6 / 20 (30.00%)	3 / 20 (15.00%)	
occurrences (all)	6	3	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 20 (5.00%)	2 / 20 (10.00%)	
occurrences (all)	1	2	
Joint stiffness			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Muscle spasms			
subjects affected / exposed	1 / 20 (5.00%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Musculoskeletal stiffness			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	2	0	
Myalgia			
subjects affected / exposed	1 / 20 (5.00%)	2 / 20 (10.00%)	
occurrences (all)	1	2	
Myositis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Pain in extremity			

subjects affected / exposed	2 / 20 (10.00%)	0 / 20 (0.00%)	
occurrences (all)	2	0	
Groin pain			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Infections and infestations			
COVID-19			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Cystitis			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Device related infection			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Pharyngitis			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 20 (5.00%)	1 / 20 (5.00%)	
occurrences (all)	1	1	
Hyperamylasaemia			
subjects affected / exposed	1 / 20 (5.00%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Hyperkalaemia			
subjects affected / exposed	0 / 20 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 February 2022	The following changes were made as per amendment 2: - It was clarified that the biopsy to be collected on Day 1 of Cycle 2 in Cohort 1 can be done up to 24 hours prior to drug administration - The eligibility requirement for aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase (ALP) was updated to clarify that the listed exceptions are specific to participants in Cohort 2 - An eligibility criterion was revised to clarify that in Cohort 2, only participants with histologically confirmed Stage IV (metastatic) cutaneous melanoma will be enrolled - Language was updated to clarify that for participants enrolled in Cohort 1, pathological tumor assessment is only performed after 6 weeks of treatment with completion lymph node dissection and radiographic tumor assessment is only required to be performed according to RECIST v1.1 at baseline and at Week 6. - Text was added to clarify that adrenocorticotropic hormone, cortisol, S100, and erythrocyte sedimentation rate (ESR) will be assessed at screening and pre-surgery only for participants enrolled in Cohort 1 - It was clarified that the pregnancy test performed at Week 13 is part of the treatment completion/discontinuation visit and not considered to be part of the follow-up period. - Timepoint for collection of blood and plasma samples for biomarker assessments during follow-up in Cohort 2 of the RO7247669 + tiragolumab arm was removed
13 December 2022	The following changes were made as per amendment 3: - The adverse event management guidelines were updated to align with the Atezolizumab Investigator’s Brochure, Version 19 and addendums. - The term, survival follow-up, was replaced with the term long-term follow up, for clarity . - Text was revised to specify that on-treatment tissue samples will be collected up to 72 hours prior to study drug administration on Day 1 of Cycle 2. - Text was added to clarify that participants with missing or no pathological response evaluation will be classified as non-responders. - The follow-up visit at 6 months was renamed Surgery Follow-Up and text was updated to clarify that this visit will occur 6 months after surgery for participants who proceed to surgery. - Text was added to clarify when a participant will return to the clinic for a treatment completion/discontinuation visit, which depends on whether or not the participant proceeds to surgery. - Text was revised to clarify that the Wald method with continuity correction will be used to calculate the difference in pathologic response rate and objective response rate

08 May 2023	The following changes were made as per amendment 4: - The RO7247669 600 mg treatment arm was for Cohort 1 to evaluate the efficacy, safety, and pharmacokinetics of a lower dose of RO7247669 based on merging data. - The RO7247669 600 mg+tiragolumab treatment arm was added for Cohort 1 to evaluate the efficacy, safety, and pharmacokinetics of a lower dose of RO7247669 in combination with tiragolumab based on emerging data. - The sample sizes was updated to 195-290 participants in Cohort 1 and 8-46 participants in Cohort 2 to reflect the number of participants currently enrolled (as of 20 March 2023) in the trial and the addition of the two new treatment arms. - Text was added to clarify that for most arms, approximately 20 participants will be enrolled during the preliminary phase. Approximately 40 participants will be enrolled in the RO7247669 600 mg and RO7247669 600 mg+tiragolumab arms during the preliminary phase to ensure a more precise benefit-risk assessment in arms with the lower dose of RO7247669. - Text was modified to clarify that participants who do not proceed to complete lymph node dissection will be classified as non-responders. - Throughout the protocol, the dose of RO7247669 was updated to indicate the use of either 2100 or 600 mg.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported