Clinical trial results:
A Phase II, Randomized, Blinded, Placebo-controlled Study of MTIG7192A, an Anti-tigit Antibody, in Combination With Atezolizumab in Chemotherapy-naive Patients With Locally Advanced or Metastatic Non-small Cell Lung Cancer

Summary

EudraCT number	2018-000280-81
Trial protocol	FR ES PL
Global end of trial date	

Results information

Result version number	v1 (current)
This version publication date	05 July 2020
First version publication date	05 July 2020

Trial information

Trial identification

Sponsor protocol code	GO40290

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03563716
WHO universal trial number (UTN)	-

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Interim
Date of interim/final analysis	30 June 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 June 2019
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

This study will evaluate the efficacy of MTIG7192A plus atezolizumab compared with placebo plus atezolizumab in chemotherapy-naive patients with locally advanced unresectable or metastatic PD-L1-selected non-small cell lung cancer (NSCLC), excluding patients with a sensitizing EGFR mutation or ALK translocation.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 August 2018
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 35
Country: Number of subjects enrolled	France: 12
Country: Number of subjects enrolled	Korea, Republic of: 30
Country: Number of subjects enrolled	Serbia: 10
Country: Number of subjects enrolled	Taiwan: 12
Country: Number of subjects enrolled	United States: 36
Worldwide total number of subjects	135
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)	56
From 65 to 84 years	79
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were recruited at study sites in 6 countries.

Pre-assignment

Screening details:

Eligible patients with previously untreated, locally advanced unresectable or metastatic PD-L1-selected non-small cell lung cancer (NSCLC) were randomized 1:1 to receive either placebo plus atezolizumab or MTIG7192A plus atezolizumab.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo + Atezolizumab

Arm description:

Participants received atezolizumab at a fixed dose of 1200 mg administered by intravenous (IV) infusion every 3 weeks (Q3W) on Day 1 of each 21-day cycle and placebo administered by IV infusion Q3W on Day 1 of each 21-day cycle.

Arm type	Placebo
Investigational medicinal product name	atezolizumab
Investigational medicinal product code	
Other name	Tecentriq
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Fixed dose of 1200 mg atezolizumab was administered by IV infusion Q3W on Day 1 of each 21-day cycle.

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Matching placebo was administered by IV infusion Q3W on Day 1 of each 21-day cycle.

Arm title	MTIG7192A + Atezolizumab

Arm description:

Participants received atezolizumab at a fixed dose of 1200 mg administered by IV infusion Q3W on Day 1 of each 21-day cycle and MTIG7192A at a dose of 600 mg administered by IV infusion Q3W on Day 1 of each 21-day cycle.

Arm type	Experimental
Investigational medicinal product name	atezolizumab
Investigational medicinal product code	
Other name	Tecentriq
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details: Fixed dose of 1200 mg atezolizumab was administered by IV infusion Q3W on Day 1 of each 21-day cycle.	
Investigational medicinal product name	MTIG7192A
Investigational medicinal product code	
Other name	tiragolumab
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: Fixed dose of 600 mg MTIG7192A was administered by IV infusion Q3W on Day 1 of each 21-day cycle.	

Number of subjects in period 1	Placebo + Atezolizumab	MTIG7192A + Atezolizumab
Started	68	67
Completed	0	0
Not completed	68	67
Still on study	45	50
Consent withdrawn by subject	3	3
Death	20	14

Baseline characteristics

Reporting groups	
Reporting group title	Placebo + Atezolizumab
Reporting group description:	
Participants received atezolizumab at a fixed dose of 1200 mg administered by intravenous (IV) infusion every 3 weeks (Q3W) on Day 1 of each 21-day cycle and placebo administered by IV infusion Q3W on Day 1 of each 21-day cycle.	
Reporting group title	MTIG7192A + Atezolizumab
Reporting group description:	
Participants received atezolizumab at a fixed dose of 1200 mg administered by IV infusion Q3W on Day 1 of each 21-day cycle and MTIG7192A at a dose of 600 mg administered by IV infusion Q3W on Day 1 of each 21-day cycle.	

Reporting group values	Placebo + Atezolizumab	MTIG7192A + Atezolizumab	Total
Number of subjects	68	67	135
Age categorical			
Units: Subjects			
Age Continuous			
Units: years			
arithmetic mean	67.0	65.8	
standard deviation	± 9.9	± 10.4	-
Sex: Female, Male			
Units:			
Male	48	39	87
Female	20	28	48

End points

End points reporting groups

Reporting group title	Placebo + Atezolizumab
Reporting group description:	
Participants received atezolizumab at a fixed dose of 1200 mg administered by intravenous (IV) infusion every 3 weeks (Q3W) on Day 1 of each 21-day cycle and placebo administered by IV infusion Q3W on Day 1 of each 21-day cycle.	
Reporting group title	MTIG7192A + Atezolizumab
Reporting group description:	
Participants received atezolizumab at a fixed dose of 1200 mg administered by IV infusion Q3W on Day 1 of each 21-day cycle and MTIG7192A at a dose of 600 mg administered by IV infusion Q3W on Day 1 of each 21-day cycle.	

Primary: Objective Response Rate (ORR)

End point title	Objective Response Rate (ORR)
End point description:	
ORR, defined as a complete response (CR) or partial response (PR) on two consecutive occasions >/=4 weeks apart, as determined by the investigator according to RECIST v1.1. CR: Disappearance of all target lesions. PR: 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. Intent-to-Treat (ITT) population included all participants randomized in the study.	
End point type	Primary
End point timeframe:	
From baseline until a total of 80 progression free survival (PFS) events have occurred (up to approximately 11 months)	

End point values	Placebo + Atezolizumab	MTIG7192A + Atezolizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	67		
Units: percentage of participants				
number (confidence interval 95%)	16.2 (6.69 to 25.66)	31.3 (19.49 to 43.20)		

Statistical analyses

Statistical analysis title	Placebo arm versus MTIG7192A arm
Statistical analysis description:	
Stratified analysis based on PD-L1 immunohistochemistry (IHC) 22C3 pharmDx, tumor histology status, and tobacco history.	
Comparison groups	Placebo + Atezolizumab v MTIG7192A + Atezolizumab

Number of subjects included in analysis	135
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Odds ratio (OR)
Point estimate	2.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.07
upper limit	6.14

Primary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)

End point description:

PFS, defined as the time from randomization to the first occurrence of disease progression (PD), as determined by the investigator according to RECIST v1.1, or death from any cause, whichever occurs first. PD: At least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum of diameters at prior timepoints (including baseline). ITT population included all participants randomized in the study. 9999=NE= not estimable

End point type	Primary

End point timeframe:

From baseline until a total of 80 PFS events have occurred (up to approximately 11 months)

End point values	Placebo + Atezolizumab	MTIG7192A + Atezolizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	68	67		
Units: months				
median (confidence interval 95%)	3.58 (2.73 to 4.44)	5.42 (4.21 to 9999)		

Statistical analyses

Statistical analysis title	Placebo arm versus MTIG7192A arm

Statistical analysis description:

Stratified analysis based on PD-L1 IHC 22C3 pharmDx, tumor histology status, and tobacco history.

Comparison groups	Placebo + Atezolizumab v MTIG7192A + Atezolizumab
Number of subjects included in analysis	135
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Hazard ratio (HR)
Point estimate	0.57

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.37
upper limit	0.9

Secondary: Duration of Objective Response (DOR)

End point title	Duration of Objective Response (DOR)

End point description:

DOR, defined as the time from the first occurrence of a documented objective response (CR or PR) to disease progression (PD), as determined by the investigator according to RECIST v1.1, or death from any cause, whichever occurs first. CR: Disappearance of all target lesions. PR: 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. PD: At least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum of diameters at prior timepoints (including baseline).

End point type	Secondary

End point timeframe:

Up to 5 years

End point values	Placebo + Atezolizumab	MTIG7192A + Atezolizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[1]	0[2]		
Units: months				
median (confidence interval 95%)	(to)	(to)		

Notes:

[1] - Data collection not complete; to be reported at time of Final Results.

[2] - Data collection not complete; to be reported at time of Final Results.

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

OS, defined as the time from randomization to death from any cause.

End point type	Secondary

End point timeframe:

Up to 5 years

End point values	Placebo + Atezolizumab	MTIG7192A + Atezolizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[3]	0[4]		
Units: months				
median (confidence interval 95%)	(to)	(to)		

Notes:

[3] - Data collection not complete; to be reported at time of Final Results.

[4] - Data collection not complete; to be reported at time of Final Results.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Adverse Events

End point title	Percentage of Participants With Adverse Events

End point description:

An adverse event is any untoward medical occurrence in a subject administered a pharmaceutical product and which does not necessarily have to have a causal relationship with the treatment. An adverse event can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a pharmaceutical product, whether or not considered related to the pharmaceutical product. Preexisting conditions which worsen during a study are also considered as adverse events.

End point type	Secondary

End point timeframe:

Up to 5 years

End point values	Placebo + Atezolizumab	MTIG7192A + Atezolizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[5]	0[6]		
Units: percentage of participants				
number (not applicable)				

Notes:

[5] - Data collection not complete; to be reported at time of Final Results.

[6] - Data collection not complete; to be reported at time of Final Results.

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Concentrations of MTIG7192A

End point title	Serum Concentrations of MTIG7192A

End point description:

End point type	Secondary

End point timeframe:

Cycle 1 Day 1, Cycle 2 Day 1, Cycle 4 Day 1, Cycle 12 Day 1 (each cycle is 21 days), at treatment discontinuation visit (up to 5 years).

End point values	Placebo + Atezolizumab	MTIG7192A + Atezolizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[7]	0[8]		
Units: microgram/milliliter (mcg/mL)				
arithmetic mean (standard deviation)	()	()		

Notes:

[7] - Data collection not complete; to be reported at time of Final Results.

[8] - Data collection not complete; to be reported at time of Final Results.

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Concentrations of Atezolizumab

End point title	Serum Concentrations of Atezolizumab

End point description:

End point type	Secondary

End point timeframe:

Cycle 1 Day 1, Cycle 2 Day 1, Cycle 4 Day 1, Cycle 12 Day 1 (each cycle is 21 days), at treatment discontinuation visit (up to 5 years).

End point values	Placebo + Atezolizumab	MTIG7192A + Atezolizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[9]	0[10]		
Units: microgram/milliliter (mcg/mL)				
arithmetic mean (standard deviation)	()	()		

Notes:

[9] - Data collection not complete; to be reported at time of Final Results.

[10] - Data collection not complete; to be reported at time of Final Results.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Treatment-Emergent Anti-Drug Antibodies (ADAs)

End point title	Percentage of Participants With Treatment-Emergent Anti-Drug Antibodies (ADAs)

End point description:

End point type	Secondary

End point timeframe:

Cycle 1 Day 1, Cycle 2 Day 1, Cycle 4 Day 1, Cycle 12 Day 1 (each cycle is 21 days), at treatment discontinuation visit (up to 5 years).

End point values	Placebo + Atezolizumab	MTIG7192A + Atezolizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[11]	0[12]		
Units: percentage of participants				
number (not applicable)				

Notes:

[11] - Data collection not complete; to be reported at time of Final Results.

[12] - Data collection not complete; to be reported at time of Final Results.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to primary completion date (approximately 11 months)	
Adverse event reporting additional description:	
The safety population included all participants who received at least one dose of study medication.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups	
Reporting group title	MTIG7192A + Atezolizumab
Reporting group description:	
Participants received atezolizumab at a fixed dose of 1200 mg administered by intravenous (IV) infusion every 3 weeks (Q3W) on Day 1 of each 21-day cycle and MTIG7192A at a dose of 600 mg administered by IV infusion Q3W on Day 1 of each 21-day cycle.	
Reporting group title	Placebo + Atezolizumab
Reporting group description:	
Participants received atezolizumab at a fixed dose of 1200 mg administered by IV infusion Q3W on Day 1 of each 21-day cycle and placebo administered by IV infusion Q3W on Day 1 of each 21-day cycle.	

Serious adverse events	MTIG7192A + Atezolizumab	Placebo + Atezolizumab	
Total subjects affected by serious adverse events			
subjects affected / exposed	23 / 67 (34.33%)	24 / 68 (35.29%)	
number of deaths (all causes)	15	20	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Pericardial effusion malignant			
subjects affected / exposed	1 / 67 (1.49%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Pelvic venous thrombosis			
subjects affected / exposed	0 / 67 (0.00%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Phlebitis			

subjects affected / exposed	1 / 67 (1.49%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vena cava thrombosis			
subjects affected / exposed	0 / 67 (0.00%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 67 (0.00%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 67 (0.00%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pain			
subjects affected / exposed	0 / 67 (0.00%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 67 (1.49%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	1 / 1	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Bronchospasm			
subjects affected / exposed	0 / 67 (0.00%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	1 / 67 (1.49%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Haemoptysis			
subjects affected / exposed	1 / 67 (1.49%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			
subjects affected / exposed	0 / 67 (0.00%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	4 / 67 (5.97%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	0 / 67 (0.00%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	1 / 67 (1.49%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 67 (0.00%)	2 / 68 (2.94%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 67 (0.00%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 67 (0.00%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Lipase increased			
subjects affected / exposed	1 / 67 (1.49%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	1 / 67 (1.49%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 67 (1.49%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardio-respiratory arrest			
subjects affected / exposed	0 / 67 (0.00%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Myocarditis			
subjects affected / exposed	0 / 67 (0.00%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia			
subjects affected / exposed	0 / 67 (0.00%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 67 (0.00%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Encephalopathy			

subjects affected / exposed	1 / 67 (1.49%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neurotoxicity			
subjects affected / exposed	0 / 67 (0.00%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 67 (0.00%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	1 / 67 (1.49%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	1 / 67 (1.49%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatitis			
subjects affected / exposed	1 / 67 (1.49%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune-mediated hepatitis			
subjects affected / exposed	0 / 67 (0.00%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	0 / 67 (0.00%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 67 (0.00%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Autoimmune nephritis			
subjects affected / exposed	1 / 67 (1.49%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydronephrosis			
subjects affected / exposed	0 / 67 (0.00%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Adrenal haemorrhage			
subjects affected / exposed	0 / 67 (0.00%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Musculoskeletal pain			
subjects affected / exposed	0 / 67 (0.00%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Cytomegalovirus colitis			
subjects affected / exposed	0 / 67 (0.00%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epstein-Barr virus infection			
subjects affected / exposed	1 / 67 (1.49%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Influenza			

subjects affected / exposed	2 / 67 (2.99%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection			
subjects affected / exposed	0 / 67 (0.00%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural infection bacterial			
subjects affected / exposed	1 / 67 (1.49%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	5 / 67 (7.46%)	4 / 68 (5.88%)	
occurrences causally related to treatment / all	0 / 5	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 1	
Respiratory tract infection			
subjects affected / exposed	0 / 67 (0.00%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin infection			
subjects affected / exposed	1 / 67 (1.49%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 67 (0.00%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 67 (1.49%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	0 / 67 (0.00%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	0 / 67 (0.00%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	1 / 67 (1.49%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	MTIG7192A + Atezolizumab	Placebo + Atezolizumab	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	60 / 67 (89.55%)	58 / 68 (85.29%)	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	17 / 67 (25.37%)	17 / 68 (25.00%)	
occurrences (all)	19	18	
Fatigue			
subjects affected / exposed	15 / 67 (22.39%)	9 / 68 (13.24%)	
occurrences (all)	18	9	
Oedema peripheral			
subjects affected / exposed	7 / 67 (10.45%)	3 / 68 (4.41%)	
occurrences (all)	10	3	
Pyrexia			
subjects affected / exposed	8 / 67 (11.94%)	9 / 68 (13.24%)	
occurrences (all)	9	12	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	6 / 67 (8.96%)	7 / 68 (10.29%)	
occurrences (all)	6	8	

Dyspnoea			
subjects affected / exposed	9 / 67 (13.43%)	13 / 68 (19.12%)	
occurrences (all)	10	15	
Haemoptysis			
subjects affected / exposed	5 / 67 (7.46%)	5 / 68 (7.35%)	
occurrences (all)	6	5	
Productive cough			
subjects affected / exposed	3 / 67 (4.48%)	7 / 68 (10.29%)	
occurrences (all)	3	7	
Rhinorrhoea			
subjects affected / exposed	4 / 67 (5.97%)	5 / 68 (7.35%)	
occurrences (all)	4	6	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	6 / 67 (8.96%)	4 / 68 (5.88%)	
occurrences (all)	6	4	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	3 / 67 (4.48%)	6 / 68 (8.82%)	
occurrences (all)	3	6	
Amylase increased			
subjects affected / exposed	4 / 67 (5.97%)	2 / 68 (2.94%)	
occurrences (all)	9	2	
Aspartate aminotransferase increased			
subjects affected / exposed	5 / 67 (7.46%)	5 / 68 (7.35%)	
occurrences (all)	5	5	
Blood creatinine increased			
subjects affected / exposed	1 / 67 (1.49%)	4 / 68 (5.88%)	
occurrences (all)	2	4	
Lipase increased			
subjects affected / exposed	4 / 67 (5.97%)	2 / 68 (2.94%)	
occurrences (all)	7	2	
Weight decreased			
subjects affected / exposed	4 / 67 (5.97%)	3 / 68 (4.41%)	
occurrences (all)	4	3	
Injury, poisoning and procedural complications			

Infusion related reaction			
subjects affected / exposed	18 / 67 (26.87%)	7 / 68 (10.29%)	
occurrences (all)	22	17	
Nervous system disorders			
Dizziness			
subjects affected / exposed	5 / 67 (7.46%)	2 / 68 (2.94%)	
occurrences (all)	5	2	
Headache			
subjects affected / exposed	4 / 67 (5.97%)	5 / 68 (7.35%)	
occurrences (all)	5	5	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	7 / 67 (10.45%)	4 / 68 (5.88%)	
occurrences (all)	7	4	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	4 / 67 (5.97%)	3 / 68 (4.41%)	
occurrences (all)	5	6	
Constipation			
subjects affected / exposed	9 / 67 (13.43%)	9 / 68 (13.24%)	
occurrences (all)	9	9	
Diarrhoea			
subjects affected / exposed	9 / 67 (13.43%)	10 / 68 (14.71%)	
occurrences (all)	12	11	
Nausea			
subjects affected / exposed	4 / 67 (5.97%)	7 / 68 (10.29%)	
occurrences (all)	4	9	
Vomiting			
subjects affected / exposed	4 / 67 (5.97%)	6 / 68 (8.82%)	
occurrences (all)	5	7	
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	13 / 67 (19.40%)	8 / 68 (11.76%)	
occurrences (all)	13	12	
Rash			
subjects affected / exposed	13 / 67 (19.40%)	6 / 68 (8.82%)	
occurrences (all)	14	7	

Rash maculo-papular			
subjects affected / exposed	6 / 67 (8.96%)	1 / 68 (1.47%)	
occurrences (all)	8	1	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	4 / 67 (5.97%)	4 / 68 (5.88%)	
occurrences (all)	4	4	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	11 / 67 (16.42%)	6 / 68 (8.82%)	
occurrences (all)	14	7	
Back pain			
subjects affected / exposed	6 / 67 (8.96%)	2 / 68 (2.94%)	
occurrences (all)	6	2	
Musculoskeletal chest pain			
subjects affected / exposed	2 / 67 (2.99%)	4 / 68 (5.88%)	
occurrences (all)	2	4	
Musculoskeletal pain			
subjects affected / exposed	4 / 67 (5.97%)	6 / 68 (8.82%)	
occurrences (all)	4	7	
Myalgia			
subjects affected / exposed	3 / 67 (4.48%)	4 / 68 (5.88%)	
occurrences (all)	3	4	
Pain in extremity			
subjects affected / exposed	5 / 67 (7.46%)	2 / 68 (2.94%)	
occurrences (all)	5	2	
Infections and infestations			
Respiratory tract infection			
subjects affected / exposed	2 / 67 (2.99%)	5 / 68 (7.35%)	
occurrences (all)	2	7	
Upper respiratory tract infection			
subjects affected / exposed	5 / 67 (7.46%)	4 / 68 (5.88%)	
occurrences (all)	5	4	
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	11 / 67 (16.42%)	12 / 68 (17.65%)	
occurrences (all)	11	12	
Hypercalcaemia			
subjects affected / exposed	0 / 67 (0.00%)	4 / 68 (5.88%)	
occurrences (all)	0	4	
Hypokalaemia			
subjects affected / exposed	4 / 67 (5.97%)	1 / 68 (1.47%)	
occurrences (all)	6	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 December 2018	The following exclusion criteria were added: 1) Patients with the pulmonary lymphoepithelioma-like carcinoma subtype of NSCLC are excluded; 2) Patients with active Epstein-Barr virus (EBV) infection and patients with known or suspected chronic active EBV infection at screening are excluded. Lists of identified risks for atezolizumab and guidelines for managing participants, who experience atezolizumab-associated adverse events, were revised to include nephritis.
06 February 2020	The potential and identified risks for MTIG7192A and atezolizumab were updated to align with Investigator's Brochures for MTIG7192A and atezolizumab. "Immune-related" was changed to "immune-mediated" when describing events associated with atezolizumab. References to the Immune-Modified Response Evaluation Criteria in Solid Tumors were removed. The timing of adverse event reporting was clarified. Systemic immune activation was replaced by hemophagocytic lymphohistiocytosis and macrophage activation syndrome in the list of potential risks for atezolizumab and the management guidelines for systemic immune activation were replaced with management guidelines for hemophagocytic lymphohistiocytosis and macrophage activation syndrome. In addition, systemic immune activation was removed from the list of adverse events of special interest.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported