



Clinical trial results:

A Phase II, Multicenter, Randomized, Placebo-Controlled, Double-Blind Study of MOXR0916 in Combination with Atezolizumab versus Atezolizumab Alone in Patients with Untreated Locally Advanced or Metastatic Urothelial Carcinoma who are Ineligible for Cisplatin-Based Therapy

Summary

EudraCT number	2016-004165-58
Trial protocol	GB BE PT FR
Global end of trial date	25 April 2018

Results information

Result version number	v1 (current)
This version publication date	10 May 2019
First version publication date	10 May 2019

Trial information

Trial identification

Sponsor protocol code	GO39590
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03029832
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	Final
Date of interim/final analysis	25 April 2018
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	25 April 2018
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

A Study of MOXR0916 in Combination with Atezolizumab versus Atezolizumab Alone in Subjects with Untreated Locally Advanced or Metastatic Urothelial Carcinoma who are Ineligible for Cisplatin-Based Therapy

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 April 2017
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	United Kingdom: 2
Country: Number of subjects enrolled	United States: 3
Worldwide total number of subjects	5
EEA total number of subjects	2

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)	1
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Only 5 subjects were recruited due to slow patient accrual and discontinuation of clinical development of MOXR0916.

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	MOXR0916 plus Atezolizumab

Arm description:

Participants were administered MOXR0916, 300 milligram (mg) and atezolizumab, 1200 mg by intravenous (IV) infusion on Day 1 of each 21-day cycle.

Arm type	Experimental
Investigational medicinal product name	MOXR0916
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

MOXR0916, 300 milligram (mg) by intravenous (IV) infusion on Day 1 of each 21-day cycle.

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

Dosage and administration details:

Atezolizumab, 1200 mg by intravenous (IV) infusion on Day 1 of each 21-day cycle.

Arm title	Atezolizumab
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Arm description:

Participants were administered atezolizumab, 1200 mg by intravenous (IV) infusion on Day 1 of each 21-day cycle.

Arm type	Active comparator
Investigational medicinal product name	Atezolizumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Atezolizumab, 1200 mg by intravenous (IV) infusion on Day 1 of each 21-day cycle.

Number of subjects in period 1	MOXR0916 plus Atezolizumab	Atezolizumab
Started	4	1
Completed	0	0
Not completed	4	1
Study Terminated By Sponsor	1	1
Safety Follow-Up Completed	2	-
Adverse event, serious fatal (disease progression)	1	-

Baseline characteristics

Reporting groups

Reporting group title	MOXR0916 plus Atezolizumab
Reporting group description:	
Participants were administered MOXR0916, 300 milligram (mg) and atezolizumab, 1200 mg by intravenous (IV) infusion on Day 1 of each 21-day cycle.	
Reporting group title	Atezolizumab
Reporting group description:	
Participants were administered atezolizumab, 1200 mg by intravenous (IV) infusion on Day 1 of each 21-day cycle.	

Reporting group values	MOXR0916 plus Atezolizumab	Atezolizumab	Total
Number of subjects	4	1	5
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	1	0	1
From 65-84 years	3	1	4
85 years and over	0	0	0
Age Continuous			
99= arbitrary value to protect subject confidentiality; 9999 = non-estimable value			
Units: years			
arithmetic mean	71.0	99	
standard deviation	± 10.6	± 9999	-
Sex: Female, Male			
Units: Subjects			
Female	2	0	2
Male	2	1	3
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	4	1	5
More than one race	0	0	0
Unknown or Not Reported	0	0	0

End points

End points reporting groups

Reporting group title	MOXR0916 plus Atezolizumab
Reporting group description:	
Participants were administered MOXR0916, 300 milligram (mg) and atezolizumab, 1200 mg by intravenous (IV) infusion on Day 1 of each 21-day cycle.	
Reporting group title	Atezolizumab
Reporting group description:	
Participants were administered atezolizumab, 1200 mg by intravenous (IV) infusion on Day 1 of each 21-day cycle.	

Primary: Progression-Free Survival (PFS)

End point title	Progression-Free Survival (PFS) ^[1]
End point description:	
PFS is defined as the time from randomization to the first occurrence of disease progression or death from any cause, whichever occurs first. Per RECIST v1.1, progressive disease is defined as at least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum of diameters on study (including baseline); and an absolute increase of ≥ 5 millimeter (mm) in the sum of diameters.	
End point type	Primary
End point timeframe:	
Up to approximately 45 months	

Notes:

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

Justification: Due to the termination of the study and small number of subjects, no analyses were performed.

End point values	MOXR0916 plus Atezolizumab	Atezolizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[2]	0 ^[3]		
Units: months				
median (confidence interval 95%)	(to)	(to)		

Notes:

[2] - Due to early termination, no formal analyses were performed for PFS and 0 subjects analyzed.

[3] - Due to early termination, no formal analyses were performed for PFS and 0 subjects analyzed.

Statistical analyses

No statistical analyses for this end point

Primary: Overall Survival (OS)

End point title	Overall Survival (OS) ^[4]
End point description:	
Kaplan Meier estimate of median OS was defined as the time at which half of the subjects had died, regardless of the cause of death.	
End point type	Primary
End point timeframe:	
Up to approximately 45 months	

Notes:

[4] - 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: Due to the termination of the study and small number of subjects, no analyses were performed.

End point values	MOXR0916 plus Atezolizumab	Atezolizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[5]	0 ^[6]		
Units: months				
median (confidence interval 95%)	(to)	(to)		

Notes:

[5] - Due to early termination, no formal analyses were performed for OS and 0 subjects analyzed.

[6] - Due to early termination, no formal analyses were performed for OS and 0 subjects analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response (OR) According to RECIST v1.1

End point title	Objective Response (OR) According to RECIST v1.1
End point description: OR is 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 is defined as the disappearance of all target lesions. PR is 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.	
End point type	Secondary
End point timeframe: Up to approximately 45 months	

End point values	MOXR0916 plus Atezolizumab	Atezolizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[7]	0 ^[8]		
Units: percentage of subjects				
number (confidence interval 95%)	(to)	(to)		

Notes:

[7] - Due to early termination, no formal analyses were performed for OR and 0 subjects analyzed.

[8] - Due to early termination, no formal analyses were performed for OR and 0 subjects analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Objective Response (DOR) According to RECIST v1.1

End point title	Duration of Objective Response (DOR) According to RECIST v1.1
End point description: DOR is defined as the time from the first occurrence of a documented objective response to disease progression or death from any cause, whichever occurs first, as determined by the investigator	

according to RECIST v1.1. Objective response is defined as a complete response (CR) or partial response (PR) on two consecutive occasions ≥ 4 weeks apart. CR is defined as the disappearance of all target lesions. PR is 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.

End point type	Secondary
End point timeframe:	
Up to approximately 45 months	

End point values	MOXR0916 plus Atezolizumab	Atezolizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[9]	0 ^[10]		
Units: months				
median (confidence interval 95%)	(to)	(to)		

Notes:

[9] - Due to early termination, no formal analyses were performed for DOR and 0 subjects analyzed.

[10] - Due to early termination, no formal analyses were performed for DOR and 0 subjects analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Pain Progression, Pain Palliation, and Fatigue Progression as Measured by Subject-Reported Severity According to the M. D. Anderson Symptom Inventory (MDASI)

End point title	Time to Pain Progression, Pain Palliation, and Fatigue Progression as Measured by Subject-Reported Severity According to the M. D. Anderson Symptom Inventory (MDASI)
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End point description:

The MDASI is a cancer-related, self-reported questionnaire consisting of 19 items assessing symptom severity and interference with different aspects of a subject's life. The MDASI items are rated from 0 to 10, with 0 indicating that the symptom is either not present or does not interfere with the subject's activities and 10 indicating that the symptom is "as bad as you can imagine" or "interfered completely" with the subject's life.

End point type	Secondary
End point timeframe:	
Up to approximately 45 months	

End point values	MOXR0916 plus Atezolizumab	Atezolizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[11]	0 ^[12]		
Units: score				

Notes:

[11] - Due to early termination, no formal analyses performed for this endpoint.

[12] - Due to early termination, no formal analyses performed for this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Reporting Symptom Interference with Daily Living at the Time of Progression According to the MDASI

End point title	Percentage of Subjects Reporting Symptom Interference with Daily Living at the Time of Progression According to the MDASI
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End point description:

The MDASI is a cancer-related, self-reported questionnaire consisting of 19 items assessing symptom severity and interference with different aspects of a participant's life. The MDASI items are rated from 0 to 10, with 0 indicating that the symptom is either not present or does not interfere with the participant's activities and 10 indicating that the symptom is "as bad as you can imagine" or "interfered completely" with the participant's life.

End point type	Secondary
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End point timeframe:

Up to approximately 45 months

End point values	MOXR0916 plus Atezolizumab	Atezolizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[13]	0 ^[14]		
Units: percentage of subjects				

Notes:

[13] - Due to early termination, no formal analyses were performed for this endpoint.

[14] - Due to early termination, no formal analyses were performed for this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Adverse Event (AEs)

End point title	Percentage of Subjects With Adverse Event (AEs)
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End point description:

An adverse event is any untoward medical occurrence, regardless of causal attribution.

End point type	Secondary
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End point timeframe:

Up to approximately 45 months

End point values	MOXR0916 plus Atezolizumab	Atezolizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[15]	0 ^[16]		
Units: subjects				

Notes:

[15] - Data were collected but are not summarized due to privacy concerns.

[16] - Data were collected but are not summarized due to privacy concerns.

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the plasma drug concentration-time curve (AUC) of MOXR0916 and Atezolizumab

End point title	Area under the plasma drug concentration-time curve (AUC) of MOXR0916 and Atezolizumab
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End point description:

AUC represents the body's exposure to an administered drug.

End point type	Secondary
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End point timeframe:

Cycle 1 (each cycle is 21 days), Day 1: predose and 30 min. after atezolizumab infusion; Cycle 1, on Days 8 and 15. Cycles 2 4, Day 1: predose and 30 min. after atezolizumab infusion. Cycles 8, 12, and 16: predose

End point values	MOXR0916 plus Atezolizumab	Atezolizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[17]	0 ^[18]		
Units: ng*day/mL				
arithmetic mean (standard deviation)	()	()		

Notes:

[17] - Due to early termination, no formal analyses were performed for any of the pharmacokinetic measures.

[18] - Due to early termination, no formal analyses were performed for any of the pharmacokinetic measures.

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Plasma Concentration (Cmax) of MOXR0916 and Atezolizumab

End point title	Maximum Plasma Concentration (Cmax) of MOXR0916 and Atezolizumab
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End point description:

Cmax refers to the maximum (or peak) serum concentration that a drug achieves in a specified compartment or test area of the body after the drug has been administered and prior to the administration of a second dose.

End point type	Secondary
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End point timeframe:

Cycle 1 (each cycle is 21 days), Day 1: predose and 30 min. after atezolizumab infusion; Cycle 1, on Days 8 and 15. Cycles 2 4, Day 1: predose and 30 min. after atezolizumab infusion. Cycles 8, 12, and 16: predose

End point values	MOXR0916 plus Atezolizumab	Atezolizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[19]	0 ^[20]		
Units: ng/mL				
arithmetic mean (standard deviation)	()	()		

Notes:

[19] - Due to early termination, no formal analyses were performed for any of the pharmacokinetic measures.

[20] - Due to early termination, no formal analyses were performed for any of the pharmacokinetic measures.

Statistical analyses

No statistical analyses for this end point

Secondary: Minimum Plasma Concentration (Cmin) of MOXR0916 and Atezolizumab

End point title	Minimum Plasma Concentration (Cmin) of MOXR0916 and Atezolizumab
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End point description:

Cmin refers to the minimum (trough) serum concentration of a drug in a specified compartment or test area of the body.

End point type	Secondary
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End point timeframe:

Cycle 1 (each cycle is 21 days), Day 1: predose and 30 min. after atezolizumab infusion; Cycle 1, on Days 8 and 15. Cycles 2 4, Day 1: predose and 30 min. after atezolizumab infusion. Cycles 8, 12, and 16: predose

End point values	MOXR0916 plus Atezolizumab	Atezolizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[21]	0 ^[22]		
Units: ng/mL				
arithmetic mean (standard deviation)	()	()		

Notes:

[21] - Due to early termination, no formal analyses were performed for any of the pharmacokinetic measures.

[22] - Due to early termination, no formal analyses were performed for any of the pharmacokinetic measures.

Statistical analyses

No statistical analyses for this end point

Secondary: Clearance of MOXR0916 and Atezolizumab

End point title	Clearance of MOXR0916 and Atezolizumab
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End point description:

Clearance of a drug is a measure of the rate at which a drug is metabolized or eliminated by normal biological processes.

End point type	Secondary
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End point timeframe:

Cycle 1 (each cycle is 21 days), Day 1: predose and 30 min. after atezolizumab infusion; Cycle 1, on

End point values	MOXR0916 plus Atezolizumab	Atezolizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[23]	0 ^[24]		
Units: CI/F				
arithmetic mean (standard deviation)	()	()		

Notes:

[23] - Due to early termination, no formal analyses were performed for any of the pharmacokinetic measures.

[24] - Due to early termination, no formal analyses were performed for any of the pharmacokinetic measures.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Anti-Therapeutic antibodies (ATAs) to MOXR0916 and Atezolizumab

End point title	Percentage of Subjects with Anti-Therapeutic antibodies (ATAs) to MOXR0916 and Atezolizumab
End point description: ATAs may be produced by the body in response to an administered drug.	
End point type	Secondary
End point timeframe: Cycles 1 - 4 and 8, 12, and 16 (each cycle is 21 days), Day 1: predose	

End point values	MOXR0916 plus Atezolizumab	Atezolizumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0 ^[25]	0 ^[26]		
Units: percentage of subjects				

Notes:

[25] - Due to early termination, no formal analyses were performed for this endpoint.

[26] - Due to early termination, no formal analyses were performed for this endpoint.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

Up to approximately 45 months

Adverse event reporting additional description:

The safety population is defined as all patients who received at least one dose of the study medication. Data were collected for the adverse events but are not being summarized due to privacy concerns with low number of patients analyzed.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	20.1
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Reporting groups

Reporting group title	MOXR0916 plus Atezolizumab
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Reporting group description:

Participants were administered MOXR0916, 300 milligram (mg) and atezolizumab, 1200 mg by intravenous (IV) infusion on Day 1 of each 21-day cycle.

Reporting group title	Atezolizumab
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Reporting group description:

Participants were administered atezolizumab, 1200 mg by intravenous (IV) infusion on Day 1 of each 21-day cycle.

Serious adverse events	MOXR0916 plus Atezolizumab	Atezolizumab	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 4 (0.00%)	0 / 1 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			

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

Non-serious adverse events	MOXR0916 plus Atezolizumab	Atezolizumab	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 4 (0.00%)	0 / 1 (0.00%)	

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: Data were collected for the adverse events but are not being summarized due to privacy concerns with low number of patients analyzed.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 December 2016	Addressed comments that were received from the United States (U.S.) Food and Drug Administration (FDA) during the review of the Investigational New Drug (IND) application.
29 September 2017	Protocol GO39590 has been amended to reflect the Sponsor's decision to halt accrual due to enrollment challenges in the context of overall clinical development considerations for MOXR0916. As only 5 patients were enrolled, this trial will not meet its scientific objectives. Hence, study procedures that are not required for safety management or assessment of clinical benefit was streamlined or modified.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported