Clinical trial results:
A Phase Ib/II Study Evaluating the Safety and Efficacy of Atezolizumab in Combination with Obinutuzumab plus Lenalidomide in Patients with Relapsed or Refractory Follicular Lymphoma.

Summary

EudraCT number	2015-002467-42
Trial protocol	FR
Global end of trial date	07 October 2020

Results information

Result version number	v2 (current)
This version publication date	30 September 2021
First version publication date	31 October 2019
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	BO29562

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02631577
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	07 October 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	07 October 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to evaluate the safety, efficacy, pharmacokinetics (PK), and immunogenicity of induction treatment consisting of atezolizumab (Atezo) in combination with obinutuzumab (G) plus lenalidomide (Len; Atezo-G-Len) in subjects with relapsed or refractory follicular lymphoma (r/r FL), followed by maintenance treatment with Atezo-G-Len in subjects who achieved a complete response (CR), a partial response (PR), or stable disease at end of induction (EOI).

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	11 January 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 24
Country: Number of subjects enrolled	United States: 14
Worldwide total number of subjects	38
EEA total number of subjects	24

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)	25
From 65 to 84 years	13
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 14 sites in France (9) and USA (5).

Pre-assignment

Screening details:

All subjects received daily low-dose aspirin (81-100 mg) during lenalidomide treatment and until 28 days after the last dose of lenalidomide. Subjects who are unable to tolerate aspirin, who have a history of thromboembolism (TE), and who are at high risk of TE, received warfarin or low-molecular-weight heparin (LMWH).

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Atezolizumab-G-lena 15mg

Arm description:

Subjects were administered obinutuzumab, atezolizumab, and 15 mg of lenalidomide

Arm type	Experimental
Investigational medicinal product name	Obinutuzumab
Investigational medicinal product code	
Other name	Gazyvaro
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects were administered obinutzumab by IV infusion at an absolute (flat) dose of 1000 mg on Days 1, 8, and 15 of the first cycle and on Day 1 of each subsequent cycle during induction treatment, and on Day 1 of every other month (i.e., every 2 months) during maintenance treatment.

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:

Subjects were administered at a flat dose of atezolizumab consisting of one of the following:
a) 840 mg every 2 weeks (Q2W) (840 mg on Days 1 and 15 of Cycles 26, given in 28-day cycles as induction treatment) and b) 1680 mg every 4 weeks (Q4W) (840 mg on Days 1 and 2 of each month, given as maintenance treatment).

Investigational medicinal product name	Lenalidomid
Investigational medicinal product code	
Other name	Revlimid
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Subjects were administered lenalidomide orally once daily on Days 1-21 of Cycles 1-6 (28-day cycles) during induction treatment and on Days 1-21 of each month during maintenance treatment. During the dose-escalation phase, lenalidomide was administered at a dose of 15 or 20 mg during induction treatment and at 10 mg during maintenance treatment. During the expansion phase, lenalidomide was administered at the recommended phase 2 dose (RP2D) during induction treatment and at 10 mg during

maintenance treatment.

Arm title	Atezolizumab-G-lena 20mg

Arm description:

Subjects were administered obinutuzumab, atezolizumab, and 20 mg of lenalidomide.

Arm type	Experimental
Investigational medicinal product name	Obinutuzumab
Investigational medicinal product code	
Other name	Gazyvaro
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects were administered obinutzumab by IV infusion at an absolute (flat) dose of 1000 mg on Days 1, 8, and 15 of the first cycle and on Day 1 of each subsequent cycle during induction treatment, and on Day 1 of every other month (i.e., every 2 months) during maintenance treatment.

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:

Subjects were administered at a flat dose of atezolizumab consisting of one of the following:
a) 840 mg Q2W (840 mg on Days 1 and 15 of Cycles 26, given in 28-day cycles as induction treatment) and b) 1680 mg Q4W (840 mg on Days 1 and 2 of each month, given as maintenance treatment).

Investigational medicinal product name	Lenalidomid
Investigational medicinal product code	
Other name	Revlimid
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Subjects were administered lenalidomide orally once daily on Days 1-21 of Cycles 1-6 (28-day cycles) during induction treatment and on Days 1-21 of each month during maintenance treatment. During the dose-escalation phase, lenalidomide was administered at a dose of 15 or 20 mg during induction treatment and at 10 mg during maintenance treatment. During the expansion phase, lenalidomide was administered at the recommended phase 2 dose (RP2D) during induction treatment and at 10 mg during maintenance treatment.

Number of subjects in period 1	Atezolizumab-G-lena 15mg	Atezolizumab-G-lena 20mg
Started	4	34
Completed	3	24
Not completed	1	10
Consent withdrawn by subject	-	3
Death	1	7

Baseline characteristics

Reporting groups	
Reporting group title	Atezolizumab-G-lena 15mg
Reporting group description:	
Subjects were administered obinutuzumab, atezolizumab, and 15 mg of lenalidomide	
Reporting group title	Atezolizumab-G-lena 20mg
Reporting group description:	
Subjects were administered obinutuzumab, atezolizumab, and 20 mg of lenalidomide.	

Reporting group values	Atezolizumab-G-lena 15mg	Atezolizumab-G-lena 20mg	Total
Number of subjects	4	34	38
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)	3	22	25
From 65-84 years	1	12	13
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	56.5	60.4	
standard deviation	± 9.1	± 9.7	-
Sex: Female, Male Units: Subjects			
Female	1	18	19
Male	3	16	19
Race/Ethnicity, Customized Units: Subjects			
Hispanic or Latino	1	0	1
Not Hispanic or Latino	3	13	16
Not Stated	0	21	21
Race/Ethnicity, Customized Units: Subjects			
Unknown	0	20	20
White	4	14	18

End points

End points reporting groups

Reporting group title	Atezolizumab-G-lena 15mg
Reporting group description:	
Subjects were administered obinutuzumab, atezolizumab, and 15 mg of lenalidomide	
Reporting group title	Atezolizumab-G-lena 20mg
Reporting group description:	
Subjects were administered obinutuzumab, atezolizumab, and 20 mg of lenalidomide.	
Subject analysis set title	Intent-to-treat (ITT) population
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
The intent-to-treat (ITT) population included all subjects enrolled in the study.	
Subject analysis set title	Safety Evaluable Population
Subject analysis set type	Safety analysis
Subject analysis set description:	
The Safety Evaluable Population that included subjects who received at least one dose of any study treatment.	
Subject analysis set title	Efficacy Evaluable Population
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
The Efficacy Evaluable population that included subjects who received at least one dose of each component of the combination. Only subjects who received lenalidomide induction at the RP2D were included in this population.	

Primary: Percentage of Subjects Achieving Complete Response (CR) at End of Induction (EOI), as Determined by the Independent Review Committee (IRC) Using Modified Lugano 2014 Criteria

End point title	Percentage of Subjects Achieving Complete Response (CR) at End of Induction (EOI), as Determined by the Independent Review Committee (IRC) Using Modified Lugano 2014 Criteria[1]
End point description:	
Complete response (CR) was evaluated through use of PET-CT scans alone, using the Modified Lugano 2014 criteria. Response was determined by the IRC. The Efficacy Evaluable population included all subjects who received at least one dose of each of the three study drugs and who received lenalidomide induction at the 20 mg recommended Phase II dose (RP2D).	
End point type	Primary
End point timeframe:	
6 months (up to clinical cut-off date (CCOD) of 23 October 2018)	

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: Only descriptive statistics was planned to be reported in the endpoint.

End point values	Efficacy Evaluable Population			
Subject group type	Subject analysis set			
Number of subjects analysed	32			
Units: Percentage				
number (confidence interval 90%)				
Positron emission-computed tomography (PET-CT)	71.9 (56.06 to 84.47)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving CR at EOI, as Determined by the Investigator Using Modified Lugano 2014 Criteria

End point title	Percentage of Subjects Achieving CR at EOI, as Determined by the Investigator Using Modified Lugano 2014 Criteria

End point description:

CR was evaluated through use of PET-CT scans, using the Modified Lugano 2014 criteria. Response was determined by the Investigator. The Efficacy Evaluable population included all subjects who received at least one dose of each of the three study drugs and who received lenalidomide induction at the 20 mg RP2D.

End point type	Secondary

End point timeframe:

6 months (up to CCOD of 23 October 2018)

End point values	Efficacy Evaluable Population			
Subject group type	Subject analysis set			
Number of subjects analysed	32			
Units: Percentage				
number (confidence interval 90%)				
Based on PET-CT	75 (59.39 to 86.91)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Achieving CR at EOI, as Determined by the IRC and Investigator Using Lugano 2014 Criteria

End point title	Percentage of Subjects Achieving CR at EOI, as Determined by the IRC and Investigator Using Lugano 2014 Criteria

End point description:

CR was evaluated through use of CT scans, using the Lugano 2014 criteria. Response was determined by the IRC and by the Investigator. The Efficacy Evaluable population included all subjects who received at least one dose of each of the three study drugs and who received lenalidomide induction at the 20 mg RP2D.

End point type	Secondary

End point timeframe:

6 months (up to CCOD of 23 October 2018)

End point values	Efficacy Evaluable Population			
Subject group type	Subject analysis set			
Number of subjects analysed	32			
Units: Percentage				
number (confidence interval 90%)				
Determined by the IRC with CT or MRI	31.3 (18.04 to 47.21)			
Determined by Investigator with CT or MRI	50 (34.41 to 65.59)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Objective Response (CR or PR) at EOI

End point title	Percentage of Subjects With Objective Response (CR or PR) at EOI

End point description:

Objective response was evaluated through use of PET-CT scans or CT scans alone, using the Lugano 2014 or modified Lugano 2014 criteria. Response was determined by the IRC and by the Investigator. he Efficacy Evaluable population included all subjects who received at least one dose of each of the three study drugs and who received lenalidomide induction at the 20 mg RP2D.

End point type	Secondary

End point timeframe:

6 months (up to CCOD of 23 October 2018)

End point values	Efficacy Evaluable Population			
Subject group type	Subject analysis set			
Number of subjects analysed	32			
Units: Percentage				
number (confidence interval 90%)				
Determined by IRC, based on Lugano 2014 - PET	81.3 (66.31 to 91.50)			
Determined by Inv., based on Lugano 2014 - PET	84.4 (69.92 to 93.63)			
Determined by IRC, based on Lugano 2014 - CT	81.3 (66.31 to 91.50)			
Determined by Inv., based on Lugano 2014 - CT	87.5 (73.64 to 95.62)			
Determined by IRC, Modified Lugano 2014 – PET-CT	78.1 (62.81 to 89.26)			
Determined by Inv, Modified Lugano 2014 – PET-CT	84.4 (69.92 to 93.63)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Best Response (CR or PR) During the Study as Determined by the Investigator on the Basis of CT Scans Alone

End point title	Percentage of Participants With Best Response (CR or PR) During the Study as Determined by the Investigator on the Basis of CT Scans Alone

End point description:

Best Response was evaluated through use of CT scans alone, using the Lugano 2014. Response was determined by the Investigator. The Efficacy Evaluable population included all subjects who received at least one dose of each of the three study drugs and who received lenalidomide induction at the 20 mg RP2D.

End point type	Secondary

End point timeframe:

Baseline up to approximately 59 months

End point values	Efficacy Evaluable Population			
Subject group type	Subject analysis set			
Number of subjects analysed	32			
Units: Percentage				
number (confidence interval 90%)				
Best Response (CR,PR)	87.5 (73.64 to 95.62)			
CR	68.8 (52.79 to 81.96)			
PR	18.8 (8.50 to 33.69)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Adverse Events and Serious Adverse Events

End point title	Percentage of Participants With Adverse Events and Serious Adverse Events

End point description:

An adverse event is any untoward medical occurrence in a participant administered a pharmaceutical product and which does not necessarily have to have a causal relationship with the treatment. An 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. The Safety Evaluable Population included participants who received at least one dose of any study treatment.

End point type	Secondary

End point timeframe:

Baseline up to approximately 59 months

End point values	Atezolizumab-G-lena 15mg	Atezolizumab-G-lena 20mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	34		
Units: Participants				
number (not applicable)				
Adverse Events	4	34		
Serious Adverse Events	2	16		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with dose-limiting toxicities (DLTs) during cycle 2 of study treatment

End point title	Number of subjects with dose-limiting toxicities (DLTs) during cycle 2 of study treatment

End point description:

Does limiting toxicity (DLT) is defined as any one of the following events occurring during Cycle 2 of treatment and assessed by the investigator as related to study treatment: - Adverse event of any grade that leads to a delay of more than 14 days at the start of the next treatment cycle; - Hematologic adverse events (neutropenia, thrombocytopenia); - Non-hematologic adverse event, except IRRs, diarrhea, nausea or vomiting. The Safety Evaluable Population included subjects who received at least one dose of any study treatment.

End point type	Secondary

End point timeframe:

Day 1 - Day 28 of second cycle

End point values	Atezolizumab-G-lena 15mg	Atezolizumab-G-lena 20mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	34		
Units: Subjects	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Serum concentration of obinutuzumab (mcg/mL)

End point title	Serum concentration of obinutuzumab (mcg/mL)

End point description:

The following abbreviations apply in the table: Ind C = Induction Cycle; D = Day; Maint M = Maintenance Month; TRTC = Study Drug Completion or Early Discontinuation; PK FU = Pharmacokinetics and Immunogenicity Follow-up; YR = Year. The Safety Evaluable Population included participants who received at least one dose of any study treatment. 9999999 = the standard deviation couldn't be calculated from the data of 1 participant.

End point type	Secondary

End point timeframe:

Baseline up to approximately 59 months

End point values	Atezolizumab-G-lena 15mg	Atezolizumab-G-lena 20mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	34		
Units: mcg/mL				
arithmetic mean (standard deviation)				
Ind C1 D1 - Predose (n=0,2)	0 (± 0)	0.634 (± 0.857)		
Ind C1 D1 - 30 min. Postdose (n=4,30)	364 (± 45.9)	375 (± 163)		
Ind C2 D1 - Predose (n=4,32)	288 (± 84.2)	392 (± 164)		
Ind C2 D1 - Postdose (n=4,31)	606 (± 62.4)	753 (± 225)		
Ind C4 D1 - Predose (n=3,25)	175 (± 38.5)	301 (± 150)		
Ind C4 D1 - Postdose (n=3,23)	509 (± 47.0)	657 (± 198)		
Ind C6 D1 - Predose (n=3,20)	230 (± 12.3)	272 (± 106)		
Ind C6 D1 - Postdose (n=3,20)	503 (± 25.5)	652 (± 177)		
Maint M1 - Predose (n=3,20)	114 (± 16.7)	201 (± 104)		
Maint M7 - Predose (n=2,17)	66.1 (± 20.4)	112 (± 52.1)		
Maint M13 - Predose (n=1,18)	77.9 (± 9999999)	104 (± 62.9)		
Maint M19 - Predose (n=2,12)	94.0 (± 24.0)	111 (± 49.8)		
TRTC (n=0,12)	0 (± 0)	148 (± 103)		
OD120FU (n=1,10)	23.3 (± 9999999)	46.2 (± 38.6)		
O1YFU (n=2,4)	46.9 (± 66.2)	57.9 (± 115)		

Statistical analyses

No statistical analyses for this end point

Secondary: Serum concentration of atezolizumab (mcg/mL)

End point title	Serum concentration of atezolizumab (mcg/mL)

End point description:

The following abbreviations apply in the table: Ind C = Induction Cycle; D = Day; Maint M = Maintenance Month; TRTC = Study Drug Completion or Early Discontinuation; PK FU = Pharmacokinetics and Immunogenicity Follow-up; YR = Year. The Safety Evaluable Population included participants who

received at least one dose of any study treatment. 9999999 = the standard deviation couldn't be calculated from the data of 1 participant.

End point type	Secondary

End point timeframe:

Baseline up to approximately 59 months

End point values	Atezolizumab-G-lena 15mg	Atezolizumab-G-lena 20mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	34		
Units: mcg/mL				
arithmetic mean (standard deviation)				
Ind C2 D1 - Predose (n=0,1)	0 (± 0)	0.184 (± 9999999)		
Ind C2 D1 - 30 min. Postdose (n=4,32)	345 (± 195)	279 (± 123)		
Ind C2 D15 - Predose (n=3,32)	73.8 (± 6.47)	90.0 (± 33.8)		
Ind C4 D1 - Predose (n=2,29)	128 (± 33.9)	226 (± 93.9)		
Ind C4 D1 - 30 min. Postdose (n=2,27)	340 (± 38.2)	477 (± 126)		
Ind C6 D1 - Predose (n=3,28)	194 (± 40.6)	279 (± 117)		
Maint M1 - Predose (n=3,27)	79.0 (± 67.6)	172 (± 76.5)		
Maint M1 - Day 2, 30 min. Postdose (n=3,23)	653 (± 106)	666 (± 185)		
Maint M4 - Predose (n=3,25)	174 (± 32.9)	292 (± 97.1)		
Maint M7 - Predose (n=2,20)	209 (± 12.7)	322 (± 109)		
Maint M13 - Predose (n=1,19)	203 (± 9999999)	309 (± 140)		
Maint M19 - Predose (n=1,11)	351 (± 9999999)	327 (± 140)		
TRTC (n=0,13)	0 (± 0)	116 (± 81.9)		
PK FU 120D (n=1,11)	46.0 (± 9999999)	38.4 (± 24.6)		
PK FU 1YR (n=0,0)	0 (± 0)	0 (± 0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Serum concentration of lenalidomide (ng/mL)

End point title	Serum concentration of lenalidomide (ng/mL)

End point description:

The following abbreviations apply in the table: Ind C = Induction Cycle; D = Day; HR = Hour. The Safety Evaluable Population included participants who received at least one dose of any study treatment.

End point type	Secondary

End point timeframe:

Baseline up to approximately 59 months

End point values	Atezolizumab-G-lena 15mg	Atezolizumab-G-lena 20mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	34		
Units: nanograms/milliliter (ng/mL)				
arithmetic mean (standard deviation)				
Ind C1 D1 - Predose (n=0,0)	0 (± 0)	0 (± 0)		
Ind C1 D15 - Predose (n=4,17)	12.6 (± 14.3)	13.0 (± 11.4)		
Ind C1 D15 - 2.0 hr. Postdose (n=4,18)	254 (± 115)	294 (± 114)		
Ind C2 D15 - Predose (n=3,21)	3.57 (± 3.25)	15.0 (± 13.0)		
Ind C2 D15 - 30 min. Postdose (n=3,19)	241 (± 116)	293 (± 233)		
Ind C2 D15 -1.0 hr. Postdose (n=3,20)	224 (± 43.1)	354 (± 120)		
Ind C2 D15 - 2.0 hr. Postdose (n=3,19)	146 (± 41.9)	262 (± 82.1)		
Ind C2 D15 - 4.0 hr. Postdose (n=3,20)	95.8 (± 18.3)	150 (± 47.1)		
Ind C2 D15 - 8.0 hr. Postdose (n=3,20)	45.9 (± 23.9)	68.4 (± 33.6)		
Ind C6 D15 - Predose (n=3,12)	5.72 (± 3.73)	9.17 (± 6.87)		
Ind C6 D15 - 2.0 hr. Postdose (n=3,12)	200 (± 57.5)	214 (± 77.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants positive for human anti-human antibodies (HAHA) to obinutuzumab

End point title	Number of participants positive for human anti-human antibodies (HAHA) to obinutuzumab

End point description:

The following abbreviations apply in the table: Ind C = Induction Cycle; D = Day; Maint M = Maintenance Month; TRTC = Study Drug Completion or Early Discontinuation; PK FU = Pharmacokinetics and Immunogenicity Follow-up; YR = Year. All baseline and post-baseline samples from participants were negative for HAHAs to obinutuzumab and the results are shown below. The Safety Evaluable Population included participants who received at least one dose of any study treatment.

End point type	Secondary

End point timeframe:

Baseline up to approximately 59 months

End point values	Atezolizumab-G-lena 15mg	Atezolizumab-G-lena 20mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	34		
Units: Participants				
number (not applicable)				
Baseline - Negative	4	34		
Ind C6 D1 - Negative	3	27		

TRTC - Negative	0	15		
OB, PK, IMMUNO FU 120D - Negative	1	11		
OB, PK, IMMUNO FU 1YR - Negative	2	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants positive for anti-therapeutic antibodies (ATAs) to atezolizumab

End point title	Number of participants positive for anti-therapeutic antibodies (ATAs) to atezolizumab

End point description:

The following abbreviations apply in the table: Ind C = Induction Cycle; D = Day; Maint M = Maintenance Month; TRTC = Study Drug Completion or Early Discontinuation; PK FU = Pharmacokinetics and Immunogenicity Follow-up; YR = Year. All baseline and post-baseline samples were negative for ATAs to atezolizumab and the results are shown below. The Safety Evaluable Population included participants who received at least one dose of any study treatment.

End point type	Secondary

End point timeframe:

Baseline up to approximately 59 months

End point values	Atezolizumab-G-lena 15mg	Atezolizumab-G-lena 20mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	34		
Units: Participants				
number (not applicable)				
Ind C2 D1 - Negative	4	31		
Ind C2 D15 - Negative	2	32		
Ind C4 D1 - Negative	3	29		
Ind C6 D1 - Negative	3	28		
Maint M1 - Negative	3	27		
Maint M4 - Negative	3	25		
Maint M7 - Negative	2	21		
Maint M13 - Negative	1	20		
Maint M19 - Negative	2	12		
TRTC - Negative	2	15		
ATEZO, PK, IMMUNO FU 120D - Negative	1	11		
ATEZO, PK, IMMUNO FU 1YR - Negative	2	3		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Baseline up to approximately 59 months	
Adverse event reporting additional description:	
The safety population included all subjects who received at least one treatment with study medication. The adverse event severity grading scale for the NCI CTCAE v4.0 was used.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups	
Reporting group title	Atezolizumab-G-lena 15mg
Reporting group description:	
Participants were administered obinutuzumab, atezolizumab, and 15 mg of lenalidomide	
Reporting group title	Atezolizumab-G-lena 20mg
Reporting group description:	
Participants were administered obinutuzumab, atezolizumab, and 20 mg of lenalidomide.	

Serious adverse events	Atezolizumab-G-lena 15mg	Atezolizumab-G-lena 20mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 4 (50.00%)	16 / 34 (47.06%)	
number of deaths (all causes)	1	7	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
MENINGIOMA			
subjects affected / exposed	0 / 4 (0.00%)	1 / 34 (2.94%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
TUMOUR FLARE			
subjects affected / exposed	0 / 4 (0.00%)	1 / 34 (2.94%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ACUTE MYELOID LEUKAEMIA			
subjects affected / exposed	0 / 4 (0.00%)	1 / 34 (2.94%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ATYPICAL FIBROXANTHOMA			

subjects affected / exposed	0 / 4 (0.00%)	1 / 34 (2.94%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
BASAL CELL CARCINOMA			
subjects affected / exposed	0 / 4 (0.00%)	1 / 34 (2.94%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
LUNG NEOPLASM MALIGNANT			
subjects affected / exposed	0 / 4 (0.00%)	1 / 34 (2.94%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
NEUROENDOCRINE CARCINOMA OF THE SKIN			
subjects affected / exposed	0 / 4 (0.00%)	1 / 34 (2.94%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
SARCOMATOID CARCINOMA			
subjects affected / exposed	0 / 4 (0.00%)	1 / 34 (2.94%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Injury, poisoning and procedural complications			
INFUSION RELATED REACTION			
subjects affected / exposed	0 / 4 (0.00%)	1 / 34 (2.94%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
LUMBAR VERTEBRAL FRACTURE			
subjects affected / exposed	0 / 4 (0.00%)	1 / 34 (2.94%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
DEEP VEIN THROMBOSIS			
subjects affected / exposed	0 / 4 (0.00%)	1 / 34 (2.94%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

ORTHOSTATIC HYPOTENSION			
subjects affected / exposed	1 / 4 (25.00%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
ISCHAEMIC STROKE			
subjects affected / exposed	0 / 4 (0.00%)	1 / 34 (2.94%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
FEBRILE NEUTROPENIA			
subjects affected / exposed	0 / 4 (0.00%)	1 / 34 (2.94%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
ADMINISTRATION SITE EXTRAVASATION			
subjects affected / exposed	0 / 4 (0.00%)	1 / 34 (2.94%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	1 / 4 (25.00%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
DYSPNOEA			
subjects affected / exposed	0 / 4 (0.00%)	1 / 34 (2.94%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
LUNG DISORDER			
subjects affected / exposed	0 / 4 (0.00%)	2 / 34 (5.88%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			

EAR INFECTION			
subjects affected / exposed	0 / 4 (0.00%)	1 / 34 (2.94%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
EPIDIDYMITIS			
subjects affected / exposed	1 / 4 (25.00%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
INFLUENZA			
subjects affected / exposed	0 / 4 (0.00%)	1 / 34 (2.94%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA PARAINFLUENZAE VIRAL			
subjects affected / exposed	1 / 4 (25.00%)	0 / 34 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CELLULITIS			
subjects affected / exposed	0 / 4 (0.00%)	1 / 34 (2.94%)	
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 / 4 (0.00%)	1 / 34 (2.94%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
DEHYDRATION			
subjects affected / exposed	1 / 4 (25.00%)	0 / 34 (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	Atezolizumab-G-lena 15mg	Atezolizumab-G-lena 20mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)	34 / 34 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
SQUAMOUS CELL CARCINOMA			
subjects affected / exposed	0 / 4 (0.00%)	2 / 34 (5.88%)	
occurrences (all)	0	4	
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	1 / 4 (25.00%)	2 / 34 (5.88%)	
occurrences (all)	1	2	
DEEP VEIN THROMBOSIS			
subjects affected / exposed	1 / 4 (25.00%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
HOT FLUSH			
subjects affected / exposed	0 / 4 (0.00%)	2 / 34 (5.88%)	
occurrences (all)	0	2	
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	0 / 4 (0.00%)	14 / 34 (41.18%)	
occurrences (all)	0	20	
AXILLARY PAIN			
subjects affected / exposed	1 / 4 (25.00%)	0 / 34 (0.00%)	
occurrences (all)	2	0	
FATIGUE			
subjects affected / exposed	1 / 4 (25.00%)	8 / 34 (23.53%)	
occurrences (all)	1	10	
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	1 / 4 (25.00%)	2 / 34 (5.88%)	
occurrences (all)	2	2	
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	1 / 4 (25.00%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
OEDEMA PERIPHERAL			
subjects affected / exposed	1 / 4 (25.00%)	5 / 34 (14.71%)	
occurrences (all)	1	8	

PERIPHERAL SWELLING			
subjects affected / exposed	0 / 4 (0.00%)	2 / 34 (5.88%)	
occurrences (all)	0	2	
PYREXIA			
subjects affected / exposed	3 / 4 (75.00%)	5 / 34 (14.71%)	
occurrences (all)	3	6	
XEROSIS			
subjects affected / exposed	0 / 4 (0.00%)	2 / 34 (5.88%)	
occurrences (all)	0	2	
MALAISE			
subjects affected / exposed	0 / 4 (0.00%)	2 / 34 (5.88%)	
occurrences (all)	0	2	
Immune system disorders			
HYPOGAMMAGLOBULINAEMIA			
subjects affected / exposed	0 / 4 (0.00%)	2 / 34 (5.88%)	
occurrences (all)	0	2	
Respiratory, thoracic and mediastinal disorders			
DYSPNOEA			
subjects affected / exposed	1 / 4 (25.00%)	5 / 34 (14.71%)	
occurrences (all)	1	5	
COUGH			
subjects affected / exposed	2 / 4 (50.00%)	12 / 34 (35.29%)	
occurrences (all)	4	14	
NASAL CONGESTION			
subjects affected / exposed	2 / 4 (50.00%)	4 / 34 (11.76%)	
occurrences (all)	2	5	
EPISTAXIS			
subjects affected / exposed	0 / 4 (0.00%)	2 / 34 (5.88%)	
occurrences (all)	0	2	
OROPHARYNGEAL PAIN			
subjects affected / exposed	1 / 4 (25.00%)	1 / 34 (2.94%)	
occurrences (all)	1	1	
PRODUCTIVE COUGH			
subjects affected / exposed	1 / 4 (25.00%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
PNEUMONITIS			

subjects affected / exposed	1 / 4 (25.00%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
RHINORRHOEA			
subjects affected / exposed	1 / 4 (25.00%)	3 / 34 (8.82%)	
occurrences (all)	1	4	
SINUS CONGESTION			
subjects affected / exposed	0 / 4 (0.00%)	2 / 34 (5.88%)	
occurrences (all)	0	2	
Psychiatric disorders			
INSOMNIA			
subjects affected / exposed	1 / 4 (25.00%)	4 / 34 (11.76%)	
occurrences (all)	1	5	
DEPRESSION			
subjects affected / exposed	2 / 4 (50.00%)	2 / 34 (5.88%)	
occurrences (all)	2	2	
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	1 / 4 (25.00%)	2 / 34 (5.88%)	
occurrences (all)	2	2	
AMYLASE INCREASED			
subjects affected / exposed	1 / 4 (25.00%)	2 / 34 (5.88%)	
occurrences (all)	2	2	
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	1 / 4 (25.00%)	2 / 34 (5.88%)	
occurrences (all)	1	2	
LIPASE INCREASED			
subjects affected / exposed	1 / 4 (25.00%)	4 / 34 (11.76%)	
occurrences (all)	2	6	
WEIGHT DECREASED			
subjects affected / exposed	1 / 4 (25.00%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
FALL			
subjects affected / exposed	1 / 4 (25.00%)	2 / 34 (5.88%)	
occurrences (all)	1	2	

INFUSION RELATED REACTION			
subjects affected / exposed	1 / 4 (25.00%)	11 / 34 (32.35%)	
occurrences (all)	2	12	
SKIN ABRASION			
subjects affected / exposed	1 / 4 (25.00%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
SPINAL COMPRESSION FRACTURE			
subjects affected / exposed	1 / 4 (25.00%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
TACHYCARDIA			
subjects affected / exposed	1 / 4 (25.00%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
DIZZINESS			
subjects affected / exposed	0 / 4 (0.00%)	3 / 34 (8.82%)	
occurrences (all)	0	4	
NEUROPATHY PERIPHERAL			
subjects affected / exposed	1 / 4 (25.00%)	2 / 34 (5.88%)	
occurrences (all)	1	3	
PARAESTHESIA			
subjects affected / exposed	1 / 4 (25.00%)	4 / 34 (11.76%)	
occurrences (all)	1	4	
POST HERPETIC NEURALGIA			
subjects affected / exposed	1 / 4 (25.00%)	1 / 34 (2.94%)	
occurrences (all)	1	1	
PERIPHERAL SENSORY NEUROPATHY			
subjects affected / exposed	1 / 4 (25.00%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
TREMOR			
subjects affected / exposed	0 / 4 (0.00%)	2 / 34 (5.88%)	
occurrences (all)	0	2	
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	1 / 4 (25.00%)	6 / 34 (17.65%)	
occurrences (all)	1	6	
LEUKOPENIA			

subjects affected / exposed	0 / 4 (0.00%)	2 / 34 (5.88%)	
occurrences (all)	0	2	
NEUTROPENIA			
subjects affected / exposed	3 / 4 (75.00%)	14 / 34 (41.18%)	
occurrences (all)	4	43	
THROMBOCYTOPENIA			
subjects affected / exposed	1 / 4 (25.00%)	9 / 34 (26.47%)	
occurrences (all)	1	14	
Ear and labyrinth disorders			
VERTIGO			
subjects affected / exposed	0 / 4 (0.00%)	2 / 34 (5.88%)	
occurrences (all)	0	2	
Eye disorders			
LACRIMATION INCREASED			
subjects affected / exposed	1 / 4 (25.00%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
DRY EYE			
subjects affected / exposed	0 / 4 (0.00%)	2 / 34 (5.88%)	
occurrences (all)	0	3	
Gastrointestinal disorders			
ABDOMINAL DISTENSION			
subjects affected / exposed	0 / 4 (0.00%)	2 / 34 (5.88%)	
occurrences (all)	0	2	
ABDOMINAL PAIN			
subjects affected / exposed	1 / 4 (25.00%)	8 / 34 (23.53%)	
occurrences (all)	2	10	
ABDOMINAL PAIN UPPER			
subjects affected / exposed	2 / 4 (50.00%)	1 / 34 (2.94%)	
occurrences (all)	3	2	
CONSTIPATION			
subjects affected / exposed	3 / 4 (75.00%)	12 / 34 (35.29%)	
occurrences (all)	5	13	
DIARRHOEA			
subjects affected / exposed	3 / 4 (75.00%)	19 / 34 (55.88%)	
occurrences (all)	9	42	
DYSPEPSIA			

subjects affected / exposed	0 / 4 (0.00%)	3 / 34 (8.82%)	
occurrences (all)	0	6	
DYSPHAGIA			
subjects affected / exposed	0 / 4 (0.00%)	2 / 34 (5.88%)	
occurrences (all)	0	2	
HAEMATOCHEZIA			
subjects affected / exposed	0 / 4 (0.00%)	2 / 34 (5.88%)	
occurrences (all)	0	2	
NAUSEA			
subjects affected / exposed	4 / 4 (100.00%)	4 / 34 (11.76%)	
occurrences (all)	4	7	
RECTAL HAEMORRHAGE			
subjects affected / exposed	1 / 4 (25.00%)	2 / 34 (5.88%)	
occurrences (all)	1	2	
STOMATITIS			
subjects affected / exposed	2 / 4 (50.00%)	0 / 34 (0.00%)	
occurrences (all)	2	0	
VOMITING			
subjects affected / exposed	4 / 4 (100.00%)	3 / 34 (8.82%)	
occurrences (all)	8	4	
HAEMORRHOIDS			
subjects affected / exposed	0 / 4 (0.00%)	4 / 34 (11.76%)	
occurrences (all)	0	6	
Hepatobiliary disorders			
CHOLECYSTITIS			
subjects affected / exposed	1 / 4 (25.00%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
HEPATOCELLULAR INJURY			
subjects affected / exposed	0 / 4 (0.00%)	3 / 34 (8.82%)	
occurrences (all)	0	4	
Skin and subcutaneous tissue disorders			
ERYTHEMA			
subjects affected / exposed	0 / 4 (0.00%)	2 / 34 (5.88%)	
occurrences (all)	0	2	
NIGHT SWEATS			

subjects affected / exposed	1 / 4 (25.00%)	4 / 34 (11.76%)	
occurrences (all)	1	4	
PRURITUS			
subjects affected / exposed	2 / 4 (50.00%)	5 / 34 (14.71%)	
occurrences (all)	2	6	
RASH			
subjects affected / exposed	0 / 4 (0.00%)	7 / 34 (20.59%)	
occurrences (all)	0	8	
RASH MACULO-PAPULAR			
subjects affected / exposed	0 / 4 (0.00%)	3 / 34 (8.82%)	
occurrences (all)	0	6	
Renal and urinary disorders			
HYDRONEPHROSIS			
subjects affected / exposed	1 / 4 (25.00%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
URINARY RETENTION			
subjects affected / exposed	1 / 4 (25.00%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
DYSURIA			
subjects affected / exposed	0 / 4 (0.00%)	3 / 34 (8.82%)	
occurrences (all)	0	3	
Endocrine disorders			
HYPERTHYROIDISM			
subjects affected / exposed	1 / 4 (25.00%)	7 / 34 (20.59%)	
occurrences (all)	1	9	
HYPOTHYROIDISM			
subjects affected / exposed	0 / 4 (0.00%)	6 / 34 (17.65%)	
occurrences (all)	0	6	
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	2 / 4 (50.00%)	7 / 34 (20.59%)	
occurrences (all)	3	10	
BACK PAIN			
subjects affected / exposed	1 / 4 (25.00%)	2 / 34 (5.88%)	
occurrences (all)	2	2	
BONE PAIN			

subjects affected / exposed	0 / 4 (0.00%)	3 / 34 (8.82%)	
occurrences (all)	0	4	
FLANK PAIN			
subjects affected / exposed	1 / 4 (25.00%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
GROIN PAIN			
subjects affected / exposed	1 / 4 (25.00%)	1 / 34 (2.94%)	
occurrences (all)	1	1	
MUSCULAR WEAKNESS			
subjects affected / exposed	1 / 4 (25.00%)	1 / 34 (2.94%)	
occurrences (all)	1	1	
MUSCLE SPASMS			
subjects affected / exposed	0 / 4 (0.00%)	8 / 34 (23.53%)	
occurrences (all)	0	15	
MUSCULOSKELETAL CHEST PAIN			
subjects affected / exposed	1 / 4 (25.00%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
MYALGIA			
subjects affected / exposed	0 / 4 (0.00%)	5 / 34 (14.71%)	
occurrences (all)	0	9	
PAIN IN EXTREMITY			
subjects affected / exposed	1 / 4 (25.00%)	5 / 34 (14.71%)	
occurrences (all)	1	5	
Infections and infestations			
BRONCHIOLITIS			
subjects affected / exposed	1 / 4 (25.00%)	0 / 34 (0.00%)	
occurrences (all)	1	0	
BRONCHITIS			
subjects affected / exposed	0 / 4 (0.00%)	10 / 34 (29.41%)	
occurrences (all)	0	13	
CONJUNCTIVITIS			
subjects affected / exposed	1 / 4 (25.00%)	2 / 34 (5.88%)	
occurrences (all)	1	2	
FUNGAL SKIN INFECTION			
subjects affected / exposed	2 / 4 (50.00%)	0 / 34 (0.00%)	
occurrences (all)	2	0	

GASTROENTERITIS				
subjects affected / exposed	1 / 4 (25.00%)	2 / 34 (5.88%)		
occurrences (all)	1	2		
HERPES ZOSTER				
subjects affected / exposed	1 / 4 (25.00%)	1 / 34 (2.94%)		
occurrences (all)	1	1		
INFLUENZA				
subjects affected / exposed	1 / 4 (25.00%)	6 / 34 (17.65%)		
occurrences (all)	1	6		
NASOPHARYNGITIS				
subjects affected / exposed	0 / 4 (0.00%)	6 / 34 (17.65%)		
occurrences (all)	0	10		
RHINITIS				
subjects affected / exposed	0 / 4 (0.00%)	9 / 34 (26.47%)		
occurrences (all)	0	12		
PHARYNGITIS				
subjects affected / exposed	0 / 4 (0.00%)	3 / 34 (8.82%)		
occurrences (all)	0	3		
SINUSITIS				
subjects affected / exposed	4 / 4 (100.00%)	7 / 34 (20.59%)		
occurrences (all)	5	13		
UPPER RESPIRATORY TRACT INFECTION				
subjects affected / exposed	1 / 4 (25.00%)	5 / 34 (14.71%)		
occurrences (all)	1	8		
TINEA INFECTION				
subjects affected / exposed	1 / 4 (25.00%)	0 / 34 (0.00%)		
occurrences (all)	1	0		
URINARY TRACT INFECTION				
subjects affected / exposed	0 / 4 (0.00%)	3 / 34 (8.82%)		
occurrences (all)	0	4		
ACUTE SINUSITIS				
subjects affected / exposed	0 / 4 (0.00%)	2 / 34 (5.88%)		
occurrences (all)	0	2		
CYSTITIS				

subjects affected / exposed	0 / 4 (0.00%)	2 / 34 (5.88%)	
occurrences (all)	0	2	
PNEUMONIA			
subjects affected / exposed	0 / 4 (0.00%)	5 / 34 (14.71%)	
occurrences (all)	0	5	
Metabolism and nutrition disorders			
FLUID OVERLOAD			
subjects affected / exposed	1 / 4 (25.00%)	0 / 34 (0.00%)	
occurrences (all)	2	0	
DECREASED APPETITE			
subjects affected / exposed	0 / 4 (0.00%)	3 / 34 (8.82%)	
occurrences (all)	0	3	
HYPERGLYCAEMIA			
subjects affected / exposed	2 / 4 (50.00%)	0 / 34 (0.00%)	
occurrences (all)	3	0	
HYPOKALAEMIA			
subjects affected / exposed	1 / 4 (25.00%)	3 / 34 (8.82%)	
occurrences (all)	2	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 June 2016	The protocol was amended in response to a health authority request. The exclusion criterion related to history of prior malignancy other than lymphoma was updated, second primary malignancies were included as events immediately reportable to the Sponsor, and the Schedule of Assessments was updated to include urinalysis and a complete physical examination on Cycle 1 Day 1.
20 September 2016	Obinutuzumab exposure data was updated to reflect the latest information from clinical studies. It was clarified that atezolizumab could be given on Day 15 of induction Cycles 2 to 6 regardless of cytopenia. Based on the latest atezolizumab Investigator's Brochure (IB; version 9), the summary of clinical safety, summary of clinical activity, the use of live vaccines after discontinuation of atezolizumab, management guidelines for non-hematologic AEs, and the list of AESIs were updated. In addition, the classification of diabetes mellitus and pancreatitis changed from 'important potential risks' to 'important identified risks'.
05 May 2017	The classification of second malignancies was changed from a selected AE to AESI to more closely monitor this AE. In addition, conditions for resuming study treatment in case of Grade >=3 laboratory abnormalities were clarified, and the list of AESIs for atezolizumab were updated to align with the latest Atezolizumab IB (version 9).
04 December 2017	On 3 July 2017, two clinical trials, KEYNOTE-183 and KEYNOTE-185, evaluating pembrolizumab (PD-1 inhibitor) in combination with an immunomodulatory agent (pomalidomide or lenalidomide) for the treatment of multiple myeloma were placed on clinical hold by the U.S. Food and Drug Administration (FDA). The clinical hold was issued because interim results demonstrated a worse overall survival in the investigational pembrolizumab arm compared to the control arm. Based on these emerging data, on 1 September 2017 the FDA also requested that other studies of PD-1/PDL-1 inhibitors and immunomodulatory agents, including study BO29562 should be placed on partial clinical hold. Although study BO29562 is conducted in a different hematologic malignancy (i.e., relapsed or refractory follicular lymphoma) and a similar safety signal has not been seen to date, the Sponsor revised the protocol to maximize patient safety. FDA removed the partial clinical hold as of 21 November 2017. Changes to the protocol, along with a rationale for each change: 1) Available Clinical Data was updated with the most recent efficacy and safety data. Stopping rules for excess toxicity and the roles of the IMC were updated, and the frequency of interim safety and efficacy analyses were amended to occur every 4 months; 2) Risks associated with obinutuzumab were updated to reflect recent updates to the obinutuzumab IB (version 12); 3) Risks associated with atezolizumab and management guidelines for atezolizumab-associated AEs were updated according to updates to the atezolizumab IB (version 10).
07 November 2018	Protocol was amended to include new safety information: 1) Lists of risks for atezolizumab and guidelines for managing patients who experience atezolizumab-associated adverse events were revised to include nephritis; 2) Considering no new safety signals have been identified with atezolizumab in combination with obinutuzumab plus lenalidomide, once all patients have completed/discontinued maintenance, regular Internal Monitoring Committee assessments would no longer take place and ad hoc meetings maybe called at the discretion of the Medical Monitor in case of newly identified safety signals; 3) Post-trial access language was changed allowing patients still under study treatment to enter an extension study in case of earlier closure of Study BO29562; 4) The Medical Monitor information was updated; 5) The Lenalidomide Summary of Product Characteristics has replaced local labels as the reference document for determining reporting requirements for single adverse events

26 October 2019	The protocol was amended to include new saftey information: 1) Background information on atezolizumab was revised to include the additional approved indications; 2) List of risks was updated to include myositis; 3) "Immune-related" was changed to "immune-mediated" when describing events associated with atezolizumab; 4) Language was added to clarify that, after withdrawal of consent for participation in the Roche Clinical Repository (RCR), remaining RCR samples were destroyed or were no longer linked to the participant; 5) To address a request by the French National Agency for the Safety of Medicines and Health Products, language regarding atezolizumab risks was revised to remove the description and management guidelines for systemic immune activation and added descriptions and management guidelines for hemophagocytic lymphohistiocytosis and macrophage activation syndrome; 6) Language was revised to account for the fact that some sites did not allow follow-up on partner pregnancies; 7) Language was updated to indicate that therapeutic or elective abortions were not considered AEs unless performed because of an underlying maternal or embryofetal toxicity; 8) Language was added for consistency with Roche's current data retention policy and to accommodate more stringent local requirements (if applicable); 9) Language was added to indicate that the study would comply with applicable local, regional, and national laws; 10) Language was revised to clarify that redacted Clinical Study Reports and other summary reports would be made available upon request; 11) Appendix 7 (Anaphylaxis Precautions) was modified to remove the requirement for use of a tourniquet; 12) Guidelines for managing participants who experienced atezolizumab-associated AEs was provided in Appendix 10.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Enrollment for this study was stopped early as the Sponsor chose not to claim superiority over existing therapies.

Notes: