Clinical trial results:
A Phase II Study Exploring the Safety and Efficacy of Atezolizumab Administered in Combination With Obinutuzumab or Rituximab Anti-CD20 Therapy in Patients With Relapsed/Refractory Mantle Cell Lymphoma, Marginal Zone Lymphoma and Waldenström Macroglobulinemia

Summary

EudraCT number	2016-003579-22
Trial protocol	ES DE LV GR SK FR IT
Global end of trial date	14 January 2022

Results information

Result version number	v1 (current)
This version publication date	29 January 2023
First version publication date	29 January 2023

Trial information

Trial identification

Sponsor protocol code	MO39107

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
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	14 January 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 January 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study evaluated the efficacy, safety and tolerability of atezolizumab in combination with obinutuzumab in participants with relapsed/refractory Mantle Cell Lymphoma (MCL) and Waldenström Macroglobulinemia (WM) or with rituximab in participants with relapsed/refractory Marginal Zone Lymphoma (MZL).

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	21 November 2017
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	24 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Bosnia and Herzegovina: 3
Country: Number of subjects enrolled	Switzerland: 1
Country: Number of subjects enrolled	Germany: 2
Country: Number of subjects enrolled	Spain: 9
Country: Number of subjects enrolled	France: 9
Country: Number of subjects enrolled	Greece: 11
Country: Number of subjects enrolled	Italy: 3
Country: Number of subjects enrolled	Latvia: 1
Country: Number of subjects enrolled	Russian Federation: 14
Country: Number of subjects enrolled	Slovakia: 2
Worldwide total number of subjects	55
EEA total number of subjects	37

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)	21
From 65 to 84 years	33
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Initially plan was to enroll 40 patients in each cohort. Enrolment was impacted by a number of limiting factors and most notably the approval of ibrutinib and the availability of this new therapy to patients, thus, sample size was reduced to a planned 30 participants in MCL cohort, 5 patients in WM cohort, and 20 patients in MZL cohort.

Pre-assignment

Screening details:

This study included participants with histologically documented, CD20 positive (assessed locally) relapsed or refractory Mantle Cell Lymphoma, Marginal Zone Lymphoma, and Waldenström's Macroglobulinemia and an Eastern Cooperative Oncology Group performance status (ECOG PS) of 0, 1, or 2 (prior to enrolment).

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 + Obinutuzumab for MCL

Arm description:

Participants with refractory or relapsed Mantle Cell Lymphoma (MCL) received atezolizumab in combination with obinutuzumab during the induction phase (Cycles 1-8), and Atezolizumab during the maintenance phase (Cycles 9-18).

Arm type	Experimental
Investigational medicinal product name	Obinutuzumab
Investigational medicinal product code	
Other name	GAZYVA
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received 1000 mg of obinutuzumab as intravenous infusions on Day 1 of each 21 day cycle for 8 cycles. Participants also received 1000 mg of obinutuzumab on Days 8 and 15 of the first cycle only. The first dose of obinutuzumab may have be split over Day 1 and Day 2 of Cycle 1 (at the discretion of the investigator).

Investigational medicinal product name	Atezolizumab
Investigational medicinal product code	
Other name	Tecentriq
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received 1200 mg of atezolizumab intravenously on Day 1 of each 21 day cycle for 8 cycles. If the first dose of obinutuzumab was split over Day 1 and Day 2 of Cycle 1, then the atezolizumab dosing occurred on Day 2 of Cycle 1, after the obinutuzumab dosing was completed. From Cycle 9, participants received 1200 mg of atezolizumab only for a further 10 cycles (to a total of 18 cycles for patients that have not progressed).

Arm title	Atezolizumab + Obinutuzumab for WM

Arm description:

Participants with Waldenström Macroglobulinemia (WM) received atezolizumab plus obinutuzumab during the induction phase (Cycles 1-8), and Atezolizumab during the maintenance phase (Cycles 9-18).

Arm type	Experimental

Investigational medicinal product name	Obinutuzumab
Investigational medicinal product code	
Other name	GAZYVA
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received 1000 mg of obinutuzumab as intravenous infusions on Day 1 of each 21 day cycle for 8 cycles. Participants also received 1000 mg of obinutuzumab on Days 8 and 15 of the first cycle only. The first dose of obinutuzumab may have be split over Day 1 and Day 2 of Cycle 1 (at the discretion of the investigator).

Investigational medicinal product name	Atezolizumab
Investigational medicinal product code	
Other name	Tecentriq
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received 1200 mg of atezolizumab intravenously on Day 1 of each 21 day cycle for 8 cycles. If the first dose of obinutuzumab was split over Day 1 and Day 2 of Cycle 1, then the atezolizumab dosing occurred on Day 2 of Cycle 1, after the obinutuzumab dosing was completed. From Cycle 9, participants received 1200 mg of atezolizumab only for a further 10 cycles (to a total of 18 cycles for patients that have not progressed).

Arm title	Atezolizumab + Rituximab for MZL

Arm description:

Participants with Marginal Zone Lymphoma (MZL) received atezolizumab in combination with rituximab during the induction phase (Cycles 1-8), and Atezolizumab during the maintenance phase (Cycles 9-18).

Arm type	Experimental
Investigational medicinal product name	Rituximab
Investigational medicinal product code	
Other name	RITUXAN
Pharmaceutical forms	Infusion, Injection
Routes of administration	Intravenous use, Subcutaneous use

Dosage and administration details:

Participants received 375mg/m2 of rituximab intravenously on Day 1 of Cycle 1. Participants also received 1400 mg of rituximab subcutaneously on Day 1 from Cycles 2-8.

Investigational medicinal product name	Atezolizumab
Investigational medicinal product code	
Other name	Tecentriq
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received 1200 mg of atezolizumab intravenously on Day 1 of Cycle 1. From Cycle 9, participants received 1200 mg of atezolizumab only for a further 10 cycles.

Number of subjects in period 1	Atezolizumab + Obinutuzumab for MCL	Atezolizumab + Obinutuzumab for WM	Atezolizumab + Rituximab for MZL
Started	30	4	21
Completed	8	1	12
Not completed	22	3	9
Physician decision	1	-	-
Consent withdrawn by subject	1	1	1

Death	16	1	7
Lost to follow-up	3	1	1
Protocol deviation	1	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Atezolizumab + Obinutuzumab for MCL
Reporting group description:	
Participants with refractory or relapsed Mantle Cell Lymphoma (MCL) received atezolizumab in combination with obinutuzumab during the induction phase (Cycles 1-8), and Atezolizumab during the maintenance phase (Cycles 9-18).	
Reporting group title	Atezolizumab + Obinutuzumab for WM
Reporting group description:	
Participants with Waldenström Macroglobulinemia (WM) received atezolizumab plus obinutuzumab during the induction phase (Cycles 1-8), and Atezolizumab during the maintenance phase (Cycles 9-18).	
Reporting group title	Atezolizumab + Rituximab for MZL
Reporting group description:	
Participants with Marginal Zone Lymphoma (MZL) received atezolizumab in combination with rituximab during the induction phase (Cycles 1-8), and Atezolizumab during the maintenance phase (Cycles 9-18).	

Reporting group values	Atezolizumab + Obinutuzumab for MCL	Atezolizumab + Obinutuzumab for WM	Atezolizumab + Rituximab for MZL
Number of subjects	30	4	21
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)	11	2	8
From 65-84 years	19	2	12
85 years and over	0	0	1
Age continuous Units: years			
arithmetic mean	67.5	62.3	68.6
standard deviation	± 8.3	± 5.6	± 11.5
Gender categorical Units: Subjects			
Female	8	2	14
Male	22	2	7

Reporting group values	Total		
Number of subjects	55		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	21		
From 65-84 years	33		
85 years and over	1		
Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	24		
Male	31		

End points

End points reporting groups

Reporting group title	Atezolizumab + Obinutuzumab for MCL
Reporting group description:	
Participants with refractory or relapsed Mantle Cell Lymphoma (MCL) received atezolizumab in combination with obinutuzumab during the induction phase (Cycles 1-8), and Atezolizumab during the maintenance phase (Cycles 9-18).	
Reporting group title	Atezolizumab + Obinutuzumab for WM
Reporting group description:	
Participants with Waldenström Macroglobulinemia (WM) received atezolizumab plus obinutuzumab during the induction phase (Cycles 1-8), and Atezolizumab during the maintenance phase (Cycles 9-18).	
Reporting group title	Atezolizumab + Rituximab for MZL
Reporting group description:	
Participants with Marginal Zone Lymphoma (MZL) received atezolizumab in combination with rituximab during the induction phase (Cycles 1-8), and Atezolizumab during the maintenance phase (Cycles 9-18).	
Subject analysis set title	Atezolizumab + Rituximab for Gastric MZL
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Gastric Marginal Zone Lymphoma (MZL) participants who received atezolizumab plus rituximab in the safety population.	
Subject analysis set title	Atezolizumab + Rituximab for Splenic MZL
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Splenic Marginal Zone Lymphoma (MZL) participants who received atezolizumab plus rituximab in the safety population.	
Subject analysis set title	Obinutuzumab Exposure for MCL
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Marginal Cell Lymphoma (MCL) participants with exposure to obinutuzumab in the safety population.	
Subject analysis set title	Atezolizumab Exposure for MCL
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Marginal Cell Lymphoma (MCL) participants with exposure to atezolizumab in the safety population.	
Subject analysis set title	Obinutuzumab Exposure for WM
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Waldenström Macroglobulinemia (WM) participants with obinutuzumab exposure in the safety population.	
Subject analysis set title	Atezolizumab Exposure for WM
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Waldenström Macroglobulinemia (WM) participants with atezolizumab exposure in the safety population.	
Subject analysis set title	Rituximab Exposure for MZL
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Marginal Zone lymphoma (MZL) participants with rituximab exposure in the safety population.	
Subject analysis set title	Atezolizumab Exposure for MZL
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Marginal Zone lymphoma (MZL) participants with atezolizumab exposure in the safety population.	

Primary: For MCL and Nodal and Extra-Nodal MZL, Objective Response at End of Induction (EOI)

End point title	For MCL and Nodal and Extra-Nodal MZL, Objective Response at End of Induction (EOI)[1][2]

End point description:

For Mantle Cell Lymphoma (MCL) and nodal and extra-nodal Marginal Zone Lymphoma (MZL), objective response at End of Induction (EOI) was defined as a Complete Response (CR) or Partial Response (PR) based on modified Cheson 2007 criteria (excluding PET).

End point type	Primary

End point timeframe:

End of induction (approximately 6 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: No statistical analysis for this end point.

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

End point values	Atezolizumab + Obinutuzumab for MCL	Atezolizumab + Rituximab for MZL		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	21		
Units: Percentage				
number (confidence interval 95%)	16.7 (5.6 to 34.7)	42.9 (21.8 to 66.0)		

Statistical analyses

No statistical analyses for this end point

Primary: Best Overall Objective Response (BOR) for WM

End point title	Best Overall Objective Response (BOR) for WM[3][4]

End point description:

For Waldenström's Macroglobulinemia (WM), Best Overall Objective Response (BOR) was defined as a Complete Response (CR), Very Good Partial Response (VGPR), Partial Response (PR), or Minimum Response (MR), based on Owen 2013 criteria, at any time during the study.

End point type	Primary

End point timeframe:

At any time during the study (up to approximately 49 months)

Notes:

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

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

End point values	Atezolizumab + Obinutuzumab for WM			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: Percentage				
number (confidence interval 95%)	0 (0.0 to 60.2)			

Statistical analyses

No statistical analyses for this end point

Primary: Objective Response at End of Induction (EOI) for Gastric MZL

End point title	Objective Response at End of Induction (EOI) for Gastric MZL[5]

End point description:

For gastric Marginal Zone Lymphoma (MZL), objective response at End of Induction (EOI), was defined as a Complete Response (CR) or Probable Minimal Residual Disease (pMRD) or Responding Residual Disease (rRD), based on the histological grading system of GELA 2003 criteria.

End point type	Primary

End point timeframe:

End of induction (approximately 6 months)

Notes:

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

End point values	Atezolizumab + Rituximab for Gastric MZL			
Subject group type	Subject analysis set			
Number of subjects analysed	3			
Units: Percentage				
number (confidence interval 95%)	66.7 (9.4 to 99.2)			

Statistical analyses

No statistical analyses for this end point

Primary: Objective Response at End of Induction (EOI) for Splenic MZL

End point title	Objective Response at End of Induction (EOI) for Splenic MZL[6]

End point description:

For splenic MZL, objective response at End of Induction (EOI) was defined as a CR or PR based on Matutes (2008).

End point type	Primary

End point timeframe:

End of induction (approximately 6 months)

Notes:

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

End point values	Atezolizumab + Rituximab for Splenic MZL			
Subject group type	Subject analysis set			
Number of subjects analysed	8			
Units: Percentage				
number (confidence interval 95%)	12.5 (0.3 to 52.7)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants with Treatment-Emergent Adverse Events

End point title	Percentage of Participants with Treatment-Emergent Adverse Events[7]

End point description:

Percentage of participants with treatment-emergent adverse events

End point type	Primary

End point timeframe:

Baseline up to to the data cutoff date: 14 January 2022 (up to approximately 49 months)

Notes:

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

End point values	Atezolizumab + Obinutuzumab for MCL	Atezolizumab + Obinutuzumab for WM	Atezolizumab + Rituximab for MZL	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	30	4	21	
Units: Percentage of participants				
number (not applicable)	93.3	100	95.2	

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival (PFS)

End point title	Progression-Free Survival (PFS)

End point description:

Progression-free survival (PFS) is defined as the time from enrolment to the first occurrence of disease progression or death from any cause, whichever occurs first, as determined by the investigator. Participants who have experienced none of these events at the time of analysis (clinical-cut off) and participants who were lost to follow-up will be censored at the time of the last evaluable tumor

assessment. Participants with no tumor assessment after the baseline visit were censored at the time of enrolment plus one day. Note: 999999=Non-Estimated.

End point type	Secondary

End point timeframe:

Enrolment to the first occurrence of disease progression or death from any cause, whichever occurs first (up to approximately 49 months).

End point values	Atezolizumab + Obinutuzumab for MCL	Atezolizumab + Obinutuzumab for WM	Atezolizumab + Rituximab for MZL	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	30	4	21	
Units: Months				
median (confidence interval 95%)	10.1 (3.4 to 14.0)	7.2 (6.2 to 999999)	23.5 (10.1 to 999999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Best Overall Response (BOR)

End point title	Best Overall Response (BOR)

End point description:

Best overall response (BOR) is defined as best response seen throughout study, of CR or PR for MCL, nodal and extra-nodal MZL and splenic MZL. CR, pMRD or rRD for gastric MZL. And for WM, this includes CR, VGPR, PR or MR.

End point type	Secondary

End point timeframe:

Throughout study (up to approximately 49 months).

End point values	Atezolizumab + Obinutuzumab for MCL	Atezolizumab + Obinutuzumab for WM	Atezolizumab + Rituximab for MZL	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	30	4	21	
Units: Percentage				
number (confidence interval 95%)	33.3 (17.3 to 52.8)	0 (0.0 to 60.2)	61.9 (38.4 to 81.9)	

Statistical analyses

No statistical analyses for this end point

Secondary: Complete Response Rate (CRR)

End point title	Complete Response Rate (CRR)

End point description:

Complete Response Rate (CRR) is defined as best response of CR.

End point type	Secondary

End point timeframe:

Throughout study (up to approximately 49 months).

End point values	Atezolizumab + Obinutuzumab for MCL	Atezolizumab + Obinutuzumab for WM	Atezolizumab + Rituximab for MZL	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	30	4	21	
Units: Percentage				
number (confidence interval 95%)	10.0 (2.1 to 26.5)	0 (0.0 to 60.2)	38.1 (18.1 to 61.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Objective Response (DOR)

End point title	Duration of Objective Response (DOR)

End point description:

Duration of objective response (DOR) is defined for responding patients as the time from first occurrence of a documented objective response to the time of progression or death from any cause, whichever occurs first, as determined by the investigator. Note: 999999=Non-Estimated.

End point type	Secondary

End point timeframe:

From first occurrence of a documented objective response to the time of progression or death from any cause (up to approximately 49 months).

End point values	Atezolizumab + Obinutuzumab for MCL	Atezolizumab + Obinutuzumab for WM	Atezolizumab + Rituximab for MZL	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5[8]	0[9]	9	
Units: Months				
median (confidence interval 95%)	999999 (999999 to 999999)	(to)	27.8 (3.4 to 999999)	

Notes:

[8] - DOR ascertained at first percentile.Of 5 responders,2 patients had events,& 3 observations censored.
[9] - The DOR was not applicable to WM patients due to no responders.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Next Treatment (TTNT)

End point title	Time to Next Treatment (TTNT)

End point description:

Time to next treatment (TTNT) is defined as the time from the date of enrolment to the start date of the next anti-lymphoma treatment (NALT) or death from any cause, whichever occurred first. Note: 999999=Non-Estimated.

End point type	Secondary

End point timeframe:

Time from the date of enrolment to the start date of the next anti-lymphoma treatment (NALT) or death from any cause, whichever occurred first (up to approximately 49 months).

End point values	Atezolizumab + Obinutuzumab for MCL	Atezolizumab + Obinutuzumab for WM	Atezolizumab + Rituximab for MZL	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	20	1[10]	12	
Units: Months				
median (confidence interval 95%)	10.5 (6.7 to 22.6)	999999 (999999 to 999999)	30.5 (16.6 to 999999)	

Notes:

[10] - As median TTNT was not established, first quartile presented was 6.2 months (95% CI: 6.2, Non-Est)..

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

Overall survival (OS) is defined as the time from enrolment to death from any cause (up to approximately 49 months). Note: 999999=Non-Estimated.

End point type	Secondary

End point timeframe:

From enrolment to death from any cause.

End point values	Atezolizumab + Obinutuzumab for MCL	Atezolizumab + Obinutuzumab for WM	Atezolizumab + Rituximab for MZL	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	30	4	21	
Units: Months				
median (confidence interval 95%)	30.9 (12.3 to 999999)	999999 (999999 to 999999)	999999 (999999 to 999999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Event-Free Survival (EFS)

End point title	Event-Free Survival (EFS)

End point description:

Event-free survival (EFS) is defined as the time from enrolment to first occurrence of disease progression or relapse, death from any cause, as assessed by the investigator, or initiation of any non-protocol-specified NALT, whichever occurred first. Note: 999999=Non-Estimated.

End point type	Secondary

End point timeframe:

From enrolment to first occurrence of disease progression or relapse, death from any cause (up to approximately 49 months).

End point values	Atezolizumab + Obinutuzumab for MCL	Atezolizumab + Obinutuzumab for WM	Atezolizumab + Rituximab for MZL	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	30	4	21	
Units: Months				
median (confidence interval 95%)	7.4 (3.4 to 12.5)	7.2 (6.2 to 999999)	23.5 (10.1 to 999999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Disease-Free Survival (DFS)

End point title	Disease-Free Survival (DFS)

End point description:

Disease-free survival (DFS) is defined as the time from the date of the first occurrence of a documented CR to the date of disease progression, relapse, or death from any cause, whichever occurred first, as assessed by the investigator, for the subgroup of patients with a BOR of CR. Note: 999999=Non-Estimated.

End point type	Secondary

End point timeframe:

From the date of the first occurrence of a documented CR to the date of disease progression, relapse, or death from any cause, whichever occurred first (up to approximately 49 months).

End point values	Atezolizumab + Obinutuzumab for MCL	Atezolizumab + Obinutuzumab for WM	Atezolizumab + Rituximab for MZL	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	3[11]	0[12]	8[13]	
Units: Months				
median (confidence interval 95%)	999999 (999999 to 999999)	(to)	999999 (999999 to 999999)	

Notes:

[11] - Due to a lack of events, only the first quartile of DFS was reached.

[12] - No patients with a best overall response of CR.

[13] - Due to a lack of events, only the first quartile of DFS was reached.

Statistical analyses

No statistical analyses for this end point

Secondary: Dose Intensity

End point title	Dose Intensity

End point description:

Dose intensity = 100 * cumulative dose / total planned dose.

End point type	Secondary

End point timeframe:

Up to approximately 49 months

End point values	Obinutuzumab Exposure for MCL	Atezolizumab Exposure for MCL	Obinutuzumab Exposure for WM	Atezolizumab Exposure for WM
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	30	30	4	4
Units: Percentage				
arithmetic mean (standard deviation)	100.0 (± 0.00)	100.0 (± 0.00)	100.0 (± 0.00)	100.0 (± 0.00)

End point values	Rituximab Exposure for MZL	Atezolizumab Exposure for MZL		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	21	21		
Units: Percentage				
arithmetic mean (standard deviation)	100.1 (± 0.21)	100.0 (± 0.00)		

Statistical analyses

No statistical analyses for this end point

Secondary: Total Number of Infusions/Injections Modified

End point title	Total Number of Infusions/Injections Modified

End point description:

Total number of infusions/injections modified (dose reductions and interruptions).

End point type	Secondary

End point timeframe:

Up to approximately 49 months

End point values	Obinutuzumab Exposure for MCL	Atezolizumab Exposure for MCL	Obinutuzumab Exposure for WM	Atezolizumab Exposure for WM
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	30	30	4	4
Units: Number of infusions/injections				
arithmetic mean (standard deviation)	0.1 (± 0.35)	0.00 (± 0.00)	0.00 (± 0.00)	0.0 (± 0.00)

End point values	Rituximab Exposure for MZL	Atezolizumab Exposure for MZL		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	21	21		
Units: Number of infusions/injections				
arithmetic mean (standard deviation)	0.2 (± 0.40)	0.0 (± 0.00)		

Statistical analyses

No statistical analyses for this end point

Secondary: Atezolizumab PK Concentration

End point title	Atezolizumab PK Concentration

End point description:

Atezolizumab PK Concentration. Note: 888888=Non-Reportable. 999999=non evaluable

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 (pre-dose and 30 minutes), Cycle 2 pre-dose, Cycle 3 pre-dose, Cycle 4 pre-dose, Cycle 8 pre-dose, Cycle 12 pre-dose, Cycle 16 pre-dose, End of treatment, Post treatment follow-up period. (Cycle length=21 days)

End point values	Atezolizumab + Obinutuzumab for MCL	Atezolizumab + Obinutuzumab for WM	Atezolizumab + Rituximab for MZL	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	28	4	21	
Units: ug/mL				
arithmetic mean (standard deviation)				
Cycle 1 Day 1/ Predose (n=28, 21, 4)	888888 (± 888888)	888888 (± 888888)	888888 (± 888888)	
Cycle 1 Day 1/ 30 Min (n=28, 21, 4)	371 (± 92.2)	308 (± 70.4)	366 (± 161)	
Cycle 2/ Predose (n=28, 20, 3)	90.4 (± 35.6)	76.5 (± 29.8)	101 (± 28.6)	
Cycle 3/ Predose (n=24, 18, 3)	176 (± 109)	138 (± 77.4)	189 (± 47.8)	
Cycle 4/ Predose (n=23, 17, 3)	209 (± 77.8)	189 (± 103)	214 (± 58.1)	
Cycle 8/ Predose (n=13, 14, 2)	303 (± 90.3)	371 (± 58.7)	297 (± 96.7)	
Cycle 12/ Predose (n=10, 14, 1)	399 (± 114)	89.7 (± 999999)	317 (± 101)	
Cycle 16/ Predose (n=8, 11, 1)	447 (± 135)	104 (± 999999)	357 (± 142)	
End of Treatment (n=23, 18, 2)	272 (± 167)	185 (± 124)	249 (± 140)	
Pose Trt FU Period (n=9, 6, 1)	67.2 (± 63.2)	2.26 (± 999999)	46.0 (± 38.0)	

Statistical analyses

No statistical analyses for this end point

Secondary: Obinutuzumab PK Concentration

End point title	Obinutuzumab PK Concentration[14]

End point description:

Obinutuzumab PK Concentration. Note: 888888=Non-Reportable

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 (pre-dose and 4 hours), Cycle 2 pre-dose, Cycle 4 pre-dose, End of treatment, Post treatment follow-up period. (Cycle length=21 days)

Notes:

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

End point values	Atezolizumab + Obinutuzumab for MCL	Atezolizumab + Obinutuzumab for WM		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	4		
Units: ug/mL				
arithmetic mean (standard deviation)				
Cycle 1 Day 1, Predose (n=27,3)	888888 (± 888888)	888888 (± 888888)		
Cycle 1 day 1,4 hours (n=24, 4)	268 (± 81.7)	231 (± 79.4)		
Cycle 2,Predose (n=27, 3)	313 (± 144)	216 (± 214)		
Cycle 4,Predose (n=22, 3)	320 (± 221)	209 (± 263)		
End of Treatment (n=14, 2)	167 (± 217)	264 (± 6.36)		

Post Trt Follow-Up Period (n=4)	31.9 (± 53.6)	888888 (± 888888)		

Statistical analyses

No statistical analyses for this end point

Secondary: Rituximab PK Concentrations

End point title	Rituximab PK Concentrations[15]

End point description:

Rituximab PK concentrations Note: 888888=non-reportable.

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 pre-dose, Cycle 1 Day 1 30 minutes, Cycle 2 pre-dose, Cycle 4 pre-dose, Cycle 8 pre-dose, End of Treatment, Post Treatment Follow-Up Period

Notes:

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

End point values	Atezolizumab + Rituximab for MZL			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: ug/mL				
arithmetic mean (standard deviation)				
Cycle 1 Day 1/pre-dose (n=21)	888888 (± 888888)			
Cycle 1 Day 1/ 30 min (n=21)	124 (± 98.2)			
Cycle 2/ pre-dose (n=20)	31.5 (± 24.1)			
Cycle 4/ pre-dose (n=18)	89.3 (± 56.7)			
Cycle 8/ pre-dose (n=14)	175 (± 64.0)			
End of Treatment (n=18)	19.7 (± 46.4)			
Post TRT FU Period (n=6)	888888 (± 888888)			

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of anti-drug antibodies (ADAs) to Atezolizumab

End point title	Incidence of anti-drug antibodies (ADAs) to Atezolizumab

End point description:

Incidence of anti-drug antibodies (ADAs) to atezolizumab.

End point type	Secondary

End point timeframe:

Baseline and Post Baseline

End point values	Atezolizumab + Obinutuzumab for MCL	Atezolizumab + Obinutuzumab for WM	Atezolizumab + Rituximab for MZL	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	28	4	21	
Units: Number of participants				
Baseline Prevalence of ADAs	0	0	1	
Post-Baseline Incidence of ADAs	1	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of anti-drug antibodies (ADAs) to Rituximab

End point title	Incidence of anti-drug antibodies (ADAs) to Rituximab[16]

End point description:

End point type	Secondary

End point timeframe:

Baseline and Post Baseline

Notes:

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

Justification: No statistical analysis for this end point.

End point values	Atezolizumab + Rituximab for MZL			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: Number of Participants				
Baseline Prevalence of ADAs	4			
Post-Baseline Incidence of ADAs	19			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the first study drug to the data cutoff date: January 14, 2022 (up to approximately 49 months)

Adverse event reporting additional description:

The safety population will include all enrolled patients who received at least one dose of study drug (atezolizumab, obinutuzumab or rituximab). Data cutoff date: 14 January 2022 (up to approximately 49 months).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18

Reporting groups

Reporting group title	Atezolizumab + Obinutuzumab for MCL

Reporting group description:

Participants with refractory or relapsed Mantle Cell Lymphoma (MCL) received atezolizumab in combination with obinutuzumab during the induction phase (Cycles 1-8), and Atezolizumab during the maintenance phase (Cycles 9-18).

Reporting group title	Atezolizumab + Rituximab for MZL

Reporting group description:

Participants with Marginal Zone Lymphoma (MZL) received atezolizumab in combination with rituximab during the induction phase (Cycles 1-8), and Atezolizumab during the maintenance phase (Cycles 9-18).

Reporting group title	Atezolizumab + Obinutuzumab for WM

Reporting group description:

Participants with Waldenström Macroglobulinemia (WM) received atezolizumab plus obinutuzumab during the induction phase (Cycles 1-8), and Atezolizumab during the maintenance phase (Cycles 9-18).

Serious adverse events	Atezolizumab + Obinutuzumab for MCL	Atezolizumab + Rituximab for MZL	Atezolizumab + Obinutuzumab for WM
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 30 (30.00%)	5 / 21 (23.81%)	0 / 4 (0.00%)
number of deaths (all causes)	16	7	1
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Hip fracture			
subjects affected / exposed	1 / 30 (3.33%)	0 / 21 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Pelvic venous thrombosis			

subjects affected / exposed	1 / 30 (3.33%)	0 / 21 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 30 (3.33%)	0 / 21 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	1 / 30 (3.33%)	0 / 21 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	1 / 30 (3.33%)	0 / 21 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Syncope			
subjects affected / exposed	1 / 30 (3.33%)	0 / 21 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 30 (0.00%)	1 / 21 (4.76%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 30 (0.00%)	1 / 21 (4.76%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			

subjects affected / exposed	0 / 30 (0.00%)	1 / 21 (4.76%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Ascites			
subjects affected / exposed	1 / 30 (3.33%)	0 / 21 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Dermatitis allergic			
subjects affected / exposed	0 / 30 (0.00%)	1 / 21 (4.76%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Infection			
subjects affected / exposed	1 / 30 (3.33%)	0 / 21 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	2 / 30 (6.67%)	1 / 21 (4.76%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Cytomegalovirus infection			
subjects affected / exposed	1 / 30 (3.33%)	0 / 21 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	2 / 30 (6.67%)	0 / 21 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	1 / 30 (3.33%)	0 / 21 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Bacterial sepsis			
subjects affected / exposed	0 / 30 (0.00%)	1 / 21 (4.76%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Atezolizumab + Obinutuzumab for MCL	Atezolizumab + Rituximab for MZL	Atezolizumab + Obinutuzumab for WM
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 30 (90.00%)	18 / 21 (85.71%)	4 / 4 (100.00%)
Vascular disorders			
Lymphoedema			
subjects affected / exposed	0 / 30 (0.00%)	0 / 21 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Phlebitis			
subjects affected / exposed	2 / 30 (6.67%)	0 / 21 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Hypotension			
subjects affected / exposed	1 / 30 (3.33%)	2 / 21 (9.52%)	0 / 4 (0.00%)
occurrences (all)	1	2	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	4 / 30 (13.33%)	2 / 21 (9.52%)	0 / 4 (0.00%)
occurrences (all)	5	2	0
Pain			
subjects affected / exposed	0 / 30 (0.00%)	2 / 21 (9.52%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Pyrexia			
subjects affected / exposed	3 / 30 (10.00%)	3 / 21 (14.29%)	0 / 4 (0.00%)
occurrences (all)	4	7	0
Fatigue			
subjects affected / exposed	2 / 30 (6.67%)	4 / 21 (19.05%)	1 / 4 (25.00%)
occurrences (all)	2	4	1
Oedema peripheral			

subjects affected / exposed	3 / 30 (10.00%)	1 / 21 (4.76%)	0 / 4 (0.00%)
occurrences (all)	3	1	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	2 / 30 (6.67%)	1 / 21 (4.76%)	0 / 4 (0.00%)
occurrences (all)	2	1	0
Cough			
subjects affected / exposed	3 / 30 (10.00%)	2 / 21 (9.52%)	2 / 4 (50.00%)
occurrences (all)	4	3	2
Rhinorrhoea			
subjects affected / exposed	3 / 30 (10.00%)	0 / 21 (0.00%)	0 / 4 (0.00%)
occurrences (all)	3	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 30 (3.33%)	2 / 21 (9.52%)	0 / 4 (0.00%)
occurrences (all)	1	2	0
Anxiety			
subjects affected / exposed	1 / 30 (3.33%)	2 / 21 (9.52%)	0 / 4 (0.00%)
occurrences (all)	1	2	0
Investigations			
Neutrophil count decreased			
subjects affected / exposed	2 / 30 (6.67%)	0 / 21 (0.00%)	1 / 4 (25.00%)
occurrences (all)	4	0	2
Lymphocyte count decreased			
subjects affected / exposed	0 / 30 (0.00%)	0 / 21 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Blood alkaline phosphatase increased			
subjects affected / exposed	2 / 30 (6.67%)	0 / 21 (0.00%)	0 / 4 (0.00%)
occurrences (all)	5	0	0
Platelet count decreased			
subjects affected / exposed	5 / 30 (16.67%)	0 / 21 (0.00%)	1 / 4 (25.00%)
occurrences (all)	7	0	1
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	0 / 30 (0.00%)	2 / 21 (9.52%)	1 / 4 (25.00%)
occurrences (all)	0	2	1

Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 30 (0.00%)	0 / 21 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 30 (6.67%)	4 / 21 (19.05%)	1 / 4 (25.00%)
occurrences (all)	2	4	1
Dizziness			
subjects affected / exposed	2 / 30 (6.67%)	1 / 21 (4.76%)	0 / 4 (0.00%)
occurrences (all)	2	2	0
Dysgeusia			
subjects affected / exposed	1 / 30 (3.33%)	2 / 21 (9.52%)	0 / 4 (0.00%)
occurrences (all)	2	2	0
Paraesthesia			
subjects affected / exposed	0 / 30 (0.00%)	2 / 21 (9.52%)	1 / 4 (25.00%)
occurrences (all)	0	2	2
Neuropathy peripheral			
subjects affected / exposed	0 / 30 (0.00%)	2 / 21 (9.52%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	6 / 30 (20.00%)	1 / 21 (4.76%)	3 / 4 (75.00%)
occurrences (all)	11	1	6
Autoimmune haemolytic anaemia			
subjects affected / exposed	0 / 30 (0.00%)	0 / 21 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Anaemia			
subjects affected / exposed	6 / 30 (20.00%)	4 / 21 (19.05%)	0 / 4 (0.00%)
occurrences (all)	8	4	0
Leukopenia			
subjects affected / exposed	1 / 30 (3.33%)	1 / 21 (4.76%)	2 / 4 (50.00%)
occurrences (all)	1	1	3
Lymphopenia			
subjects affected / exposed	1 / 30 (3.33%)	0 / 21 (0.00%)	1 / 4 (25.00%)
occurrences (all)	1	0	1
Iron deficiency anaemia			

subjects affected / exposed	1 / 30 (3.33%)	0 / 21 (0.00%)	1 / 4 (25.00%)
occurrences (all)	1	0	3
Febrile neutropenia			
subjects affected / exposed	2 / 30 (6.67%)	0 / 21 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Neutropenia			
subjects affected / exposed	6 / 30 (20.00%)	3 / 21 (14.29%)	1 / 4 (25.00%)
occurrences (all)	12	5	1
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 21 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Vertigo			
subjects affected / exposed	0 / 30 (0.00%)	0 / 21 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Toothache			
subjects affected / exposed	2 / 30 (6.67%)	1 / 21 (4.76%)	0 / 4 (0.00%)
occurrences (all)	2	1	0
Dyspepsia			
subjects affected / exposed	1 / 30 (3.33%)	1 / 21 (4.76%)	1 / 4 (25.00%)
occurrences (all)	1	1	1
Diarrhoea			
subjects affected / exposed	3 / 30 (10.00%)	3 / 21 (14.29%)	0 / 4 (0.00%)
occurrences (all)	5	3	0
Vomiting			
subjects affected / exposed	2 / 30 (6.67%)	3 / 21 (14.29%)	0 / 4 (0.00%)
occurrences (all)	2	3	0
Constipation			
subjects affected / exposed	1 / 30 (3.33%)	2 / 21 (9.52%)	1 / 4 (25.00%)
occurrences (all)	1	2	1
Hepatobiliary disorders			
Hepatitis toxic			
subjects affected / exposed	0 / 30 (0.00%)	0 / 21 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			

Rash			
subjects affected / exposed	1 / 30 (3.33%)	2 / 21 (9.52%)	0 / 4 (0.00%)
occurrences (all)	1	2	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	2 / 30 (6.67%)	0 / 21 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	2 / 30 (6.67%)	1 / 21 (4.76%)	0 / 4 (0.00%)
occurrences (all)	2	1	0
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	0 / 30 (0.00%)	0 / 21 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Arthralgia			
subjects affected / exposed	2 / 30 (6.67%)	3 / 21 (14.29%)	1 / 4 (25.00%)
occurrences (all)	2	7	1
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 30 (3.33%)	2 / 21 (9.52%)	0 / 4 (0.00%)
occurrences (all)	1	3	0
Urinary tract infection			
subjects affected / exposed	2 / 30 (6.67%)	0 / 21 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Upper respiratory tract infection			
subjects affected / exposed	2 / 30 (6.67%)	0 / 21 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Bronchitis			
subjects affected / exposed	3 / 30 (10.00%)	1 / 21 (4.76%)	0 / 4 (0.00%)
occurrences (all)	3	1	0
Pharyngitis			
subjects affected / exposed	0 / 30 (0.00%)	0 / 21 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Respiratory tract infection			

subjects affected / exposed	3 / 30 (10.00%)	0 / 21 (0.00%)	0 / 4 (0.00%)
occurrences (all)	3	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 30 (3.33%)	2 / 21 (9.52%)	0 / 4 (0.00%)
occurrences (all)	1	2	0
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	2 / 30 (6.67%)	0 / 21 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Decreased appetite			
subjects affected / exposed	1 / 30 (3.33%)	0 / 21 (0.00%)	1 / 4 (25.00%)
occurrences (all)	1	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 November 2018	Protocol was amended to include adjustment to the study sample size, and to clarify that access to atezolizumab is only within the 18 cycles of study treatment per the study design. In addition, several clarifications have been made relating to the conduct of the study and to update all safety, efficacy, and licensing status text for atezolizumab, obinutuzumab, and rituximab.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported