Clinical trial results:
A Phase IB/II Study Evaluating the Safety and Efficacy of Atezolizumab in Combination With Either Obinutuzumab Plus Bendamustine or Obinutuzumab Plus CHOP in Patients with Follicular Lymphoma or Rituximab Plus CHOP in Patients With Diffuse Large B-Cell Lymphoma

Summary

EudraCT number	2015-001364-19
Trial protocol	IT
Global end of trial date	08 May 2020

Results information

Result version number	v2 (current)
This version publication date	12 May 2021
First version publication date	25 April 2019
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	BO29563

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02596971
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	08 May 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	08 May 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

A Study of Atezolizumab in Combination With Either Obinutuzumab Plus Bendamustine or Obinutuzumab Plus (+) Cyclophosphamide, Doxorubicin, Vincristine, and Prednisone (CHOP) in Participants With Follicular Lymphoma (FL) or Rituximab + CHOP in Participants With Diffuse Large B-Cell Lymphoma (DLBCL)

Protection of trial subjects:

Each subject, or the subject's representative, signed an informed consent form prior to screening.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 December 2015
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	Australia: 14
Country: Number of subjects enrolled	Italy: 16
Country: Number of subjects enrolled	United States: 61
Worldwide total number of subjects	91
EEA total number of subjects	16

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)	61
From 65 to 84 years	30

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 15 sites in 3 countries (Italy, Australia, and USA).

Pre-assignment

Screening details:

Out of the 117 subjects who were screened for this study, 91 subjects were enrolled to either FL treatment cohort (Atezo-G-Benda, Atezo-G-CHOP) or DLBCL cohort (Atezo-R-CHOP) and 26 subjects failed screening.

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	Atezo-G-Benda Cohort (Safety Run-In and Expansion Phases)

Arm description:

Safety run-in phase: Participants with previously untreated or relapsed or refractory FL received obinutuzumab (G) and bendamustine during Cycle 1 (28-day cycle) and atezolizumab, obinutuzumab, and bendamustine during Cycles 2-6, during induction treatment, followed by atezolizumab (once monthly) and obinutuzumab (every other month [q2m]) for 24 months, during maintenance treatment. Expansion phase: Participants with previously untreated FL received same treatment regimen as described for safety run-in phase.

Arm type	Experimental
Investigational medicinal product name	Atezolizumab
Investigational medicinal product code	
Other name	RO5541267; Tecentriq
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Atezolizumab 840 milligrams (mg) intravenously (IV) on Days 1 and 15 of Cycles 2-6, during induction treatment, followed by 840 mg IV on Days 1 and 2 of each month, starting with Month 1, during maintenance treatment.

Investigational medicinal product name	Obinutuzumab
Investigational medicinal product code	
Other name	GA101, RO5072759
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Obinutuzumab administered at a dose of 1000 mg IV on Days 1, 8, and 15 of Cycle 1 and 1000 mg IV on Day 1 of Cycles 2-6, during induction treatment, followed by 1000 mg IV on Day 1 of every other month, starting with Month 1, during maintenance treatment.

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

Dosage and administration details:

Bendamustine administered at a dose of 90 milligrams per square meter (mg/m^2) IV on Days 1 and 2 of Cycles 1-6, during induction treatment.

Arm title	Atezo-G-CHOP Cohort (Safety Run-In Phase)

Arm description:

Safety run-in phase: Participants with previously untreated or relapsed or refractory FL received obinutuzumab and CHOP during Cycle 1 (21-day cycle) and atezolizumab, obinutuzumab, and CHOP during Cycles 2-6, during induction treatment, followed by atezolizumab (once monthly) and obinutuzumab (q2m) for 24 months, during maintenance treatment.

Arm type	Experimental
Investigational medicinal product name	Atezolizumab
Investigational medicinal product code	
Other name	RO5541267; Tecentriq
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Atezolizumab 1200 mg IV on Day 1 Cycles 2-6, during induction treatment, followed by 840 mg IV on Days 1 and 2 of each month, starting with Month 1.

Investigational medicinal product name	Obinutuzumab
Investigational medicinal product code	
Other name	GA101, RO5072759
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Obinutuzumab administered at a dose of 1000 mg IV on Days 1, 8, and 15 of Cycle 1 and 1000 mg IV on Day 1 of Cycles 2-6 during induction treatment, followed by 1000 mg IV on Day 1 of every other month, starting with Month 1 during maintenance treatment.

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

Dosage and administration details:

Cyclophosphamide 750 milligrams per square metre (mg/m^2), administered intravenously (IV) on Day 1 of each 21-day cycle.

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

Dosage and administration details:

Doxorubicin will be administered at a dose of 50 mg/m^2 IV on Day 1 of Cycle 1-6/8, during induction treatment.

Investigational medicinal product name	Prednisone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Prednisone will be administered at a dose of 40 mg/m^2 orally on Days 1-5 of Cycle 1-6/8, during induction treatment. Prednisolone may be given if prednisone is unavailable. The 40 mg/m^2 dose of prednisone on Day 1 will be replaced by oral corticosteroids given as premedication on Day 1 of Cycle 1 (and subsequent cycles).

Arm title	Atezo-R-CHOP Cohort (Expansion Phase)

Arm description:

Participants with previously untreated DLBCL received rituximab and CHOP during Cycle 1 (21-day cycle) and atezolizumab, rituximab, and CHOP during Cycles 2-8 (atezolizumab and rituximab for 8 cycles and CHOP for either 6 or 8 cycles, as determined by the investigator), during induction treatment,

followed by atezolizumab from Cycles 9-25 during consolidation treatment.

Arm type	Experimental
Investigational medicinal product name	Atezolizumab
Investigational medicinal product code	
Other name	RO5541267; Tecentriq
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Atezolizumab 1200 mg IV on Day 1 Cycles 2-8, during induction treatment, followed by 1200 mg IV on Day 1 of Cycles 9-25.

Investigational medicinal product name	Cyclophosphamide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intraventricular use , Intravenous use

Dosage and administration details:

Cyclophosphamide will be administered at a dose of 750 mg/m^2 IV on Day 1 of Cycle 1-6/8, during induction treatment.

Investigational medicinal product name	Prednisone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Prednisone will be administered at a dose of 40 mg/m^2 orally on Days 1-5 of Cycle 1-6/8, during induction treatment. Prednisolone may be given if prednisone is unavailable. The 40 mg/m^2 dose of prednisone on Day 1 will be replaced by oral corticosteroids given as premedication on Day 1 of Cycle 1 (and subsequent cycles).

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

Dosage and administration details:

Doxorubicin will be administered at a dose of 50 mg/m^2 IV on Day 1 of Cycle 1-6/8, during induction treatment.

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

Dosage and administration details:

Participants with previously untreated DLBCL will receive rituximab at a dose of 375 mg/m^2 IV on Day 1 of Cycle 1-8, during induction treatment.

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

Dosage and administration details:

Vincristine will be administered at a dose of 1.4 mg/m^2 (maximum 2 mg) IV on Day 1 of Cycle 1-6/8, during induction treatment.

Number of subjects in period 1	Atezo-G-Benda Cohort (Safety Run-In and Expansion Phases)	Atezo-G-CHOP Cohort (Safety Run-In Phase)	Atezo-R-CHOP Cohort (Expansion Phase)
Started	42	7	42
Completed	32	5	33
Not completed	10	2	9
Consent withdrawn by subject	5	1	4
Death	5	1	5

Baseline characteristics

Reporting groups	
Reporting group title	Atezo-G-Benda Cohort (Safety Run-In and Expansion Phases)
Reporting group description:	
Safety run-in phase: Participants with previously untreated or relapsed or refractory FL received obinutuzumab (G) and bendamustine during Cycle 1 (28-day cycle) and atezolizumab, obinutuzumab, and bendamustine during Cycles 2-6, during induction treatment, followed by atezolizumab (once monthly) and obinutuzumab (every other month [q2m]) for 24 months, during maintenance treatment. Expansion phase: Participants with previously untreated FL received same treatment regimen as described for safety run-in phase.	
Reporting group title	Atezo-G-CHOP Cohort (Safety Run-In Phase)
Reporting group description:	
Safety run-in phase: Participants with previously untreated or relapsed or refractory FL received obinutuzumab and CHOP during Cycle 1 (21-day cycle) and atezolizumab, obinutuzumab, and CHOP during Cycles 2-6, during induction treatment, followed by atezolizumab (once monthly) and obinutuzumab (q2m) for 24 months, during maintenance treatment.	
Reporting group title	Atezo-R-CHOP Cohort (Expansion Phase)
Reporting group description:	
Participants with previously untreated DLBCL received rituximab and CHOP during Cycle 1 (21-day cycle) and atezolizumab, rituximab, and CHOP during Cycles 2-8 (atezolizumab and rituximab for 8 cycles and CHOP for either 6 or 8 cycles, as determined by the investigator), during induction treatment, followed by atezolizumab from Cycles 9-25 during consolidation treatment.	

Reporting group values	Atezo-G-Benda Cohort (Safety Run-In and Expansion Phases)	Atezo-G-CHOP Cohort (Safety Run-In Phase)	Atezo-R-CHOP Cohort (Expansion Phase)
Number of subjects	42	7	42
Age Categorical Units: Subjects			
<=18 years	0	0	0
Between 18 and 65 years	35	6	20
>=65 years	7	1	22
Age Continuous Units: years			
arithmetic mean	55.6	57.4	59.2
standard deviation	± 10.9	± 5.4	± 15.7
Sex: Female, Male Units: Subjects			
Female	20	4	16
Male	22	3	26
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	3	0	2
Not Hispanic or Latino	36	7	37
Unknown or Not Reported	3	0	3
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	3	1	0
Native Hawaiian or Other Pacific Islander	0	0	0

Black or African American	0	0	0
White	37	6	40
More than one race	0	0	0
Unknown or Not Reported	2	0	2

Reporting group values	Total		
Number of subjects	91		
Age Categorical Units: Subjects			
<=18 years	0		
Between 18 and 65 years	61		
>=65 years	30		
Age Continuous Units: years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male Units: Subjects			
Female	40		
Male	51		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	5		
Not Hispanic or Latino	80		
Unknown or Not Reported	6		
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0		
Asian	4		
Native Hawaiian or Other Pacific Islander	0		
Black or African American	0		
White	83		
More than one race	0		
Unknown or Not Reported	4		

End points

End points reporting groups

Reporting group title	Atezo-G-Benda Cohort (Safety Run-In and Expansion Phases)

Reporting group description:

Safety run-in phase: Participants with previously untreated or relapsed or refractory FL received obinutuzumab (G) and bendamustine during Cycle 1 (28-day cycle) and atezolizumab, obinutuzumab, and bendamustine during Cycles 2-6, during induction treatment, followed by atezolizumab (once monthly) and obinutuzumab (every other month [q2m]) for 24 months, during maintenance treatment. Expansion phase: Participants with previously untreated FL received same treatment regimen as described for safety run-in phase.

Reporting group title	Atezo-G-CHOP Cohort (Safety Run-In Phase)

Reporting group description:

Safety run-in phase: Participants with previously untreated or relapsed or refractory FL received obinutuzumab and CHOP during Cycle 1 (21-day cycle) and atezolizumab, obinutuzumab, and CHOP during Cycles 2-6, during induction treatment, followed by atezolizumab (once monthly) and obinutuzumab (q2m) for 24 months, during maintenance treatment.

Reporting group title	Atezo-R-CHOP Cohort (Expansion Phase)

Reporting group description:

Participants with previously untreated DLBCL received rituximab and CHOP during Cycle 1 (21-day cycle) and atezolizumab, rituximab, and CHOP during Cycles 2-8 (atezolizumab and rituximab for 8 cycles and CHOP for either 6 or 8 cycles, as determined by the investigator), during induction treatment, followed by atezolizumab from Cycles 9-25 during consolidation treatment.

Primary: Percentage of Participants With 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 Participants With Complete Response (CR) at End of Induction (EOI), as Determined by the Independent Review Committee (IRC) Using Modified Lugano 2014 Criteria[1][2]

End point description:

Primary end point was positron emission tomography (PET) CR at EOI by IRC according to modified Lugano classification using PET/CT scan. CR was defined as a score of 1 (no uptake above background), 2 (uptake less than or equal to [</=] mediastinum), or 3 (uptake less than [<] mediastinum but </=liver) with or without a residual mass on PET 5-point scale (5-PS), for lymph nodes and extralymphatic sites; no new lesions; no evidence of fluorodeoxyglucose (FDG)-avid disease in bone marrow; and normal/immunohistochemistry (IHC)-negative bone marrow morphology. All positron emission tomography (PET) evaluable 1L FL and 1L DLBCL patients with at least one dose of atezolizumab were included in efficacy population.

End point type	Primary

End point timeframe:

Up to 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: Results were reported descriptively and were not planned to be analyzed for statistically significant differences between groups.
[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: Results were reported descriptively and were not planned to be analyzed for statistically significant differences between groups.

End point values	Atezo-G-Benda Cohort (Safety Run-In and Expansion Phases)	Atezo-R-CHOP Cohort (Expansion Phase)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40[3]	40[4]		
Units: percentage of participants				
number (confidence interval 90%)	75 (61.29 to 85.76)	77.5 (64.02 to 87.73)		

Notes:

[3] - 2 subjects excluded from Atezo-G-Benda cohort due to diagnosis of r/r FL.

[4] - 2 subjects excluded as they were excluded prior to Cycle 2 and were not treated with atezolizumab.

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With Adverse Events

End point title	Percentage of Participants With Adverse Events[5]

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.

End point type	Primary

End point timeframe:

Baseline up to approximately 4 years

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: This is an adverse event endpoint and did not report statistics.

End point values	Atezo-G-Benda Cohort (Safety Run-In and Expansion Phases)	Atezo-G-CHOP Cohort (Safety Run-In Phase)	Atezo-R-CHOP Cohort (Expansion Phase)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	42	7	42	
Units: percentage of participants	100	100	100	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With CR at EOI, as Determined by the Investigator Using Lugano 2014 Criteria

End point title	Percentage of Participants With CR at EOI, as Determined by the Investigator Using Lugano 2014 Criteria[6]

End point description:

Tumor response assessment was performed by the investigator according to modified Lugano

classification using PET/CT scan. CR was defined as a score of 1 (no uptake above background), 2 (uptake </=mediastinum), or 3 (uptake <mediastinum but </=liver) with or without a residual mass on PET 5-PS, for lymph nodes and extralymphatic sites; no new lesions; no evidence of FDG-avid disease in bone marrow; and normal/IHC-negative bone marrow morphology. 90% CI for percentage of responders was calculated using Clopper-Pearson method. All positron emission tomography (PET) evaluable 1L FL and 1L DLBCL subjects with at least one dose of atezolizumab were included in efficacy population.

End point type	Secondary

End point timeframe:

Up to approximately 6 months

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Results were reported descriptively and were not planned to be analyzed for statistically significant differences between groups.

End point values	Atezo-G-Benda Cohort (Safety Run-In and Expansion Phases)	Atezo-R-CHOP Cohort (Expansion Phase)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40[7]	40[8]		
Units: percentage of participants				
number (confidence interval 90%)	87.5 (75.50 to 94.94)	77.5 (64.02 to 87.73)		

Notes:

[7] - 2 subjects excluded from Atezo-G-Benda cohort due to diagnosis of r/r FL.

[8] - 2 subjects excluded as they were excluded prior to Cycle 2 and were not treated with atezolizumab.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With CR at EOI, as Determined by the IRC Using Modified Cheson 2007 Criteria

End point title	Percentage of Participants With CR at EOI, as Determined by the IRC Using Modified Cheson 2007 Criteria[9]

End point description:

Complete response according to the modified Cheson 2007 criteria using PET/CT scan: complete disappearance of all detectable clinical evidence of disease and disease-related symptoms if present prior to therapy, liver and spleen have returned to normal size (if enlarged at baseline), If the bone marrow was involved by lymphoma prior to treatment, the infiltrate must have cleared on repeat bone marrow biopsy. PR: at least 50% regression of measurable disease compared to tumors measured by a baseline scan and no new sites; no increase in the size of the other nodes, liver, or spleen; with the exception of splenic and hepatic nodules, involvement of other organs is usually assessable and no measurable disease should be present. All positron emission tomography (PET) evaluable 1L FL and 1L DLBCL subjects with at least one dose of atezolizumab were included in efficacy population.

End point type	Secondary

End point timeframe:

Up to approximately 6 months

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Results were reported descriptively and were not planned to be analyzed for statistically significant differences between groups.

End point values	Atezo-G-Benda Cohort (Safety Run-In and Expansion Phases)	Atezo-R-CHOP Cohort (Expansion Phase)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40[10]	40[11]		
Units: percentage of participants				
number (confidence interval 90%)	75.0 (61.29 to 85.76)	77.5 (64.02 to 87.73)		

Notes:

[10] - 2 subjects excluded from Atezo-G-Benda cohort due to diagnosis of r/r FL.

[11] - 2 subjects excluded as they were excluded prior to Cycle 2 and were not treated with atezolizumab.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With CR at EOI, as Determined by the Investigator Using Modified Cheson 2007 Criteria

End point title	Percentage of Participants With CR at EOI, as Determined by the Investigator Using Modified Cheson 2007 Criteria[12]

End point description:

Complete response according to modified Cheson 2007 criteria using PET/CT scan: complete disappearance of all detectable clinical evidence of disease and disease-related symptoms if present prior to therapy, liver and spleen have returned to normal size (if enlarged at baseline), If bone marrow was involved by lymphoma prior to treatment, infiltrate must have cleared on repeat bone marrow biopsy. PR: at least 50% regression of measurable disease compared to tumors measured by a baseline scan and no new sites; no increase in the size of other nodes, liver, or spleen; with exception of splenic and hepatic nodules, involvement of other organs is usually assessable and no measurable disease should be present. All positron emission tomography (PET) evaluable 1L FL and 1L DLBCL subjects with at least one dose of atezolizumab were included in efficacy population.

End point type	Secondary

End point timeframe:

Up to approximately 6 months

Notes:

[12] - 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: Results were reported descriptively and were not planned to be analyzed for statistically significant differences between groups.

End point values	Atezo-G-Benda Cohort (Safety Run-In and Expansion Phases)	Atezo-R-CHOP Cohort (Expansion Phase)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40[13]	40[14]		
Units: percentage of participants				
number (confidence interval 90%)	80.0 (66.80 to 89.64)	75.0 (61.29 to 85.76)		

Notes:

[13] - 2 subjects excluded from Atezo-G-Benda cohort due to diagnosis of r/r FL.

[14] - 2 subjects excluded as they were excluded prior to Cycle 2 and were not treated with atezolizumab.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Objective Response (CR or PR) at EOI, as Determined by the IRC Using Modified Cheson 2007 Criteria

End point title	Percentage of Participants With Objective Response (CR or PR) at EOI, as Determined by the IRC Using Modified Cheson 2007 Criteria[15]

End point description:

Objective response: having CR or PR as assessed according to the modified response criteria for iNHL (Modified Cheson et al, 2007). CR: Complete disappearance of all detectable clinical evidence of disease and disease-related symptoms if present prior to therapy, liver and spleen have returned to normal size (if enlarged at baseline), If the bone marrow was involved by lymphoma prior to treatment, the infiltrate must have cleared on repeat bone marrow biopsy. PR: at least 50% regression of measurable disease compared to tumors measured by a baseline scan and no new sites; no increase in the size of the other nodes, liver, or spleen; with the exception of splenic and hepatic nodules, involvement of other organs is usually assessable and no measurable disease should be present. All positron emission tomography (PET) evaluable 1L FL and 1L DLBCL subjects with at least one dose of atezolizumab were included in efficacy population.

End point type	Secondary

End point timeframe:

Up to approximately 6 months

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Results were reported descriptively and were not planned to be analyzed for statistically significant differences between groups.

End point values	Atezo-G-Benda Cohort (Safety Run-In and Expansion Phases)	Atezo-R-CHOP Cohort (Expansion Phase)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40[16]	40[17]		
Units: percentage of participants				
number (confidence interval 90%)	90.0 (78.56 to 96.51)	90.0 (78.56 to 96.51)		

Notes:

[16] - 2 subjecnts excluded from Atezo-G-Benda cohort due to diagnosis of r/r FL.

[17] - 2 subjects excluded as they were excluded prior to Cycle 2 and were not treated with atezolizumab.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Objective Response (CR or PR) at EOI, as Determined by the Investigator Using Modified Cheson 2007 Criteria

End point title	Percentage of Participants With Objective Response (CR or PR) at EOI, as Determined by the Investigator Using Modified Cheson 2007 Criteria[18]

End point description:

Objective response: having CR or PR as assessed according to the modified response criteria for iNHL (Modified Cheson et al, 2007). CR: Complete disappearance of all detectable clinical evidence of disease and disease-related symptoms if present prior to therapy, liver and spleen have returned to normal size (if enlarged at baseline), If the bone marrow was involved by lymphoma prior to treatment, the infiltrate must have cleared on repeat bone marrow biopsy. PR: at least 50% regression of measurable disease compared to tumors measured by a baseline scan and no new sites; no increase in the size of the other nodes, liver, or spleen; with the exception of splenic and hepatic nodules, involvement of other organs is

usually assessable and no measurable disease should be present. All positron emission tomography (PET) evaluable 1L FL and 1L DLBCL subjects with at least one dose of atezolizumab were included in efficacy population.

End point type	Secondary

End point timeframe:

Up to approximately 6 months

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Results were reported descriptively and were not planned to be analyzed for statistically significant differences between groups.

End point values	Atezo-G-Benda Cohort (Safety Run-In and Expansion Phases)	Atezo-R-CHOP Cohort (Expansion Phase)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40[19]	40[20]		
Units: percentage of participants				
number (confidence interval 90%)	95.0 (85.08 to 99.10)	87.5 (75.50 to 94.94)		

Notes:

[19] - 2 subjects excluded from Atezo-G-Benda cohort due to diagnosis of r/r FL.

[20] - 2 subjects excluded as they were excluded prior to Cycle 2 and were not treated with atezolizumab.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Objective Response (CR or PR) at EOI, as Determined by the IRC Using Lugano 2014 Criteria

End point title	Percentage of Participants With Objective Response (CR or PR) at EOI, as Determined by the IRC Using Lugano 2014 Criteria[21]

End point description:

Tumor response assessment was performed by IRC according to modified Lugano classification using PET/CT scan. OR defined as a response of CR or PR. CR: a score of 1 (no uptake above background), 2 (uptake </=mediastinum), or 3 (uptake <mediastinum but </=liver) with/without a residual mass on PET 5-PS, for lymph nodes and extralymphatic sites; no new lesions; no evidence of FDG-avid disease in bone marrow; and normal/IHC-negative bone marrow morphology. PR: a score 4 (uptake moderately greater than [>] liver) or 5 (uptake markedly >liver and/or new lesions) with reduced uptake compared with baseline and residual mass(es) of any size on PET 5-PS for lymph nodes and extralymphatic sites; no new lesions; and reduced residual uptake in bone marrow compared with baseline. All positron emission tomography (PET) evaluable 1L FL and 1L DLBCL subjects with at least one dose of atezolizumab were included in efficacy population.

End point type	Secondary

End point timeframe:

Up to approximately 6 months

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Results were reported descriptively and were not planned to be analyzed for statistically significant differences between groups.

End point values	Atezo-G-Benda Cohort (Safety Run-In and Expansion Phases)	Atezo-R-CHOP Cohort (Expansion Phase)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40[22]	40[23]		
Units: percentage of participants				
number (confidence interval 90%)	90.0 (78.56 to 96.51)	87.5 (75.50 to 94.94)		

Notes:

[22] - 2 subjects excluded from Atezo-G-Benda cohort due to diagnosis of r/r FL.

[23] - 2 subjects excluded as they were excluded prior to Cycle 2 and were not treated with atezolizumab.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Objective Response (CR or PR) at EOI, as Determined by the Investigator Using Lugano 2014 Criteria

End point title	Percentage of Participants With Objective Response (CR or PR) at EOI, as Determined by the Investigator Using Lugano 2014 Criteria[24]

End point description:

Tumor response assessment was performed by investigator according to modified Lugano classification using PET/CT scan. OR: a response of CR or PR. CR: a score of 1 (no uptake above background), 2 (uptake </=mediastinum), or 3 (uptake <mediastinum but </=liver) with or without a residual mass on PET 5-PS, for lymph nodes & extralymphatic sites; no new lesions; no evidence of FDG-avid disease in bone marrow; and normal/IHC-negative bone marrow morphology. PR with a score 4 (uptake moderately greater than [>] liver) or 5 (uptake markedly >liver and/or new lesions) with reduced uptake compared with baseline and residual mass(es) of any size on PET 5-PS for lymph nodes and extralymphatic sites; no new lesions; and reduced residual uptake in bone marrow compared with baseline. All positron emission tomography (PET) evaluable 1L FL and 1L DLBCL subjects with at least one dose of atezolizumab were included in efficacy population.

End point type	Secondary

End point timeframe:

Up to approximately 6 months

Notes:

[24] - 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: Results were reported descriptively and were not planned to be analyzed for statistically significant differences between groups.

End point values	Atezo-G-Benda Cohort (Safety Run-In and Expansion Phases)	Atezo-R-CHOP Cohort (Expansion Phase)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40[25]	40[26]		
Units: percentage of participants				
number (confidence interval 90%)	95.0 (85.08 to 99.10)	87.5 (75.50 to 94.94)		

Notes:

[25] - 2 subjects excluded from Atezo-G-Benda cohort due to diagnosis of r/r FL.

[26] - 2 subjects excluded as they were excluded prior to Cycle 2 and were not treated with atezolizumab.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Best Response of CR or PR During Study, as Determined by Investigator Using Modified Cheson 2007 Criteria

End point title	Percentage of Participants With Best Response of CR or PR During Study, as Determined by Investigator Using Modified Cheson 2007 Criteria[27]

End point description:

CR: Complete disappearance of all detectable clinical evidence of disease and disease-related symptoms if present prior to therapy, liver and spleen have returned to normal size (if enlarged at baseline), If the bone marrow was involved by lymphoma prior to treatment, the infiltrate must have cleared on repeat bone marrow biopsy. PR: at least 50% regression of measurable disease compared to tumors measured by a baseline scan and no new sites; no increase in the size of the other nodes, liver, or spleen; with the exception of splenic and hepatic nodules, involvement of other organs is usually assessable and no measurable disease should be present. Only Atezo-G-Benda and Atezo-R-Chop cohorts were evaluated for efficacy.

End point type	Secondary

End point timeframe:

Baseline up to approximately 4 years (assessed at Baseline, 6 to 8 weeks after Day [D] 1 of Cycle [Cy] 6 or 8 (1Cy: 21 or 28 days), then every 2 months up to 24 months, at 35 days of last dose, and at every 3 months post-treatment follow-up [up 4 years])

Notes:

[27] - 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: Results were reported descriptively and were not planned to be analyzed for statistically significant differences between groups.

End point values	Atezo-G-Benda Cohort (Safety Run-In and Expansion Phases)	Atezo-R-CHOP Cohort (Expansion Phase)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	40		
Units: percentage of participants				
number (confidence interval 90%)	80.0 (66.80 to 89.64)	75.0 (61.29 to 85.76)		

Statistical analyses

No statistical analyses for this end point

Secondary: Observed Serum Obinutuzumab Concentration

End point title	Observed Serum Obinutuzumab Concentration[28]

End point description:

Predose time point was "any time prior to dose" for Cycle 1 and "within 5 hour prior to dose" for other cycles (Cycles 2,5,6) and for Months 1 to 24 during maintenance phase. Infusion duration for administration of first infusion should begin at an initial rate of 50 milligrams per hour (mg/hour). If no reaction occurs, increase the infusion rate in 100 mg/hour increments every 30 minutes to a maximum of 400 mg/hour.

End point type	Secondary

End point timeframe:

Induction: Predose, 0.5 hour (h) postinfusion on D1 of Cy1,2,5,6 (1Cy: 21/28 days); Maintenance:

Predose, 0.5h postinfusion on Day 1 of Month 1,3,7,15,23; 120 days & 1 year of last dose or at treatment discontinuation (up to 4 years)

Notes:

[28] - 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: This is a pharmacokinetic endpoint and did not report statistics.

End point values	Atezo-G-Benda Cohort (Safety Run-In and Expansion Phases)	Atezo-G-CHOP Cohort (Safety Run-In Phase)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	7		
Units: ug/mL				
median (full range (min-max))				
C1 Cmax after 1st infusion (n=35, 5)	329 (21.7 to 513)	400 (284 to 450)		
C1 Cmin after the last infusion on C1 (n=39, 7)	322 (168 to 486)	399 (236 to 611)		
C6 - Cmax after last dosing of induction (n=20, 7)	544 (387 to 883)	659 (287 to 838)		
C6 - Cmin after last dosing of induction (n=22, 7)	203 (137 to 471)	245 (171 to 481)		

Statistical analyses

No statistical analyses for this end point

Secondary: Observed Serum Atezolizumab Concentration

End point title	Observed Serum Atezolizumab Concentration

End point description:

Atezo-G-Benda: Induction:Predose on D1 of Cy5,6 & D1,15 of Cy2,3 (1Cy:21/28 days), Cy2D1:0.5h postinfusion; Maintenance:Predose on D1 of Month 1,2,4,7,15,23, Month 2 D1: 0.5h postinfusion; 120 days & 1 year of last dose or at treatment discontinuation (up to 4 years); Atezo-G-CHOP: Induction:Predose on D1 of Cy2,3,5,6 (1Cy:21 days), Cy2D1:0.5h postinfusion; Maintenance:Predose on D1 of Month 1,2,3,4,7,15,23, Month 2 D1: 0.5h postinfusion; 120 days & 1 year of last dose or at treatment discontinuation (up to 4 years). Predose time point was "within 5 hour prior to dose" for Cy2,3,5,6 during induction phase and for Months 1 to 24 during maintenance phase. infusion length: 30-60 minutes. 0 represents no data was collected at that cycle.

End point type	Secondary

End point timeframe:

Atezo-R-CHOP: Predose on D1 of Cy2,3,5,8,9,10,11,12,16,20,25 (1Cy:21 days), 0.5h postinfusion of D1 of Cy2,9; at 120 days & 1 year of last dose or at treatment discontinuation (up to 4 years)

End point values	Atezo-G-Benda Cohort (Safety Run-In and Expansion Phases)	Atezo-G-CHOP Cohort (Safety Run-In Phase)	Atezo-R-CHOP Cohort (Expansion Phase)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	42	7	42	
Units: ug/mL				
median (full range (min-max))				
Cycle 2 - Cmax after 1st infusion (n=31, 31, 7)	275 (193 to 388)	424 (340 to 670)	332 (227 to 472)	
C2 - Cmin before 2nd infusion (n=32, 34, 6)	83 (59 to 128)	94 (65 to 139)	82.1 (55.7 to 122)	
C6 - Cmin aftter 6th infusion (n=20, 0, 6)	256 (93 to 369)	195 (157 to 296)	0 (0 to 0)	
C8 - Cmax after 7th infusion (n=0, 22, 0)	0 (0 to 0)	0 (0 to 0)	486.5 (363 to 793)	
C8 - Cmin before 8th infusion (n=0, 23, 0)	0 (0 to 0)	0 (0 to 0)	184 (104 to 359)	

Statistical analyses

No statistical analyses for this end point

Secondary: Observed Serum Rituximab Concentration

End point title	Observed Serum Rituximab Concentration[29]

End point description:

Predose time point was "any time prior to dose" for Cycle 1 and "within 5 hour prior to dose" for other cycles (Cycles 2,5,8) during induction phase and for Months 1 to 24 during maintenance phase. Infusion duration for administration of first infusion should begin at an initial rate of 50 mg/hour. If no infusion-related or hypersensitivity reaction occurs, increase the infusion rate in 50 mg/hour increments every 30 minutes to a maximum of 400 mg/hour. If no reaction occurs, increase the infusion rate in 100 mg/hour increments every 30 minutes to a maximum of 400 mg/hour.

End point type	Secondary

End point timeframe:

Predose, 0.5h postinfusion on D1 of Cy1,2,5,8 (1Cy: 21 days); at 120 days and 1 year after last rituximab dose or at treatment discontinuation (up to 4 years)

Notes:

[29] - 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: This is a pharmacokinetic endpoint and did not report statistics.

End point values	Atezo-R-CHOP Cohort (Expansion Phase)			
Subject group type	Reporting group			
Number of subjects analysed	42			
Units: ug/mL				
median (full range (min-max))				
C1 - Cmax after dosing C1 (n=34)	159 (0.5 to 292)			
C1 - Ctrough after dosing C1 (n=34)	26.1 (0.5 to 41.3)			

C8 - Cmax after dosing C8 (n=27)	229 (185 to 303)			
C8 - Ctrough after dosing C8 (n=26)	105.5 (39.9 to 150)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Human Anti-Human Antibodies (HAHAs) to Obinutuzumab

End point title	Percentage of Participants With Human Anti-Human Antibodies (HAHAs) to Obinutuzumab[30]

End point description:

Induction: Predose (any time prior to dose) on D1 of Cy1,5,6 (1Cy: 21/28 days); Maintenance: Predose (any time prior to dose) on D1 of Month 1; at 120 days and 1 year of last obinutuzumab dose or at treatment discontinuation (up to 4 years)

End point type	Secondary

End point timeframe:

Baseline up to approximately 4 years

Notes:

[30] - 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: Results were reported descriptively and were not planned to be analyzed for statistically significant differences between groups.

End point values	Atezo-G-Benda Cohort (Safety Run-In and Expansion Phases)			
Subject group type	Reporting group			
Number of subjects analysed	42			
Units: percentage of participants				
number (not applicable)				
Induction Cycle 1 Day 1 (n=42)	2.4			
Induction Cycle 5 Day 1 (n=31)	0			
Induction Cycle 6 Day 1 (n=34)	0			
Maintenance Month 1 (n=37)	0			
Study Drug Completion or Early Discon. (n=14)	0			
Obinutuzumab Day 120 Follow up (n=33)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Human Anti-Chimeric Antibodies (HACAs) to Rituximab

End point title	Percentage of Participants With Human Anti-Chimeric Antibodies (HACAs) to Rituximab[31]

End point description:

Induction: Predose (any time prior to dose) on D1 of Cy2,3,5,8 (1Cy: 21 days); Maintenance: Predose (any time prior to dose) on D1 of Month 1; at 120 days and 1 year of last rituximab dose or at treatment discontinuation (up to 4 years)

End point type	Secondary

End point timeframe:

Baseline up to approximately 4 years

Notes:

[31] - 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: Results were reported descriptively and were not planned to be analyzed for statistically significant differences between groups.

End point values	Atezo-R-CHOP Cohort (Expansion Phase)			
Subject group type	Reporting group			
Number of subjects analysed	42			
Units: percentage of participants				
number (not applicable)				
Baseline (n=35)	14.3			
Induction Cycle 1 Day 1 (n=2)	0			
Induction Cycle 5 Day 1 (n=36)	0			
Induction Cycle 8 Day 1 (n=28)	0			
Rituximab Day 120 Follow up (n=6)	0			
Rituximab 1 Year Follow up (n=11)	0			
Study Drug Completion or Early Discon. (n=13)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Anti-Therapeutic Antibodies (ATAs) to Atezolizumab

End point title	Percentage of Participants With Anti-Therapeutic Antibodies (ATAs) to Atezolizumab

End point description:

Atezo-G-CHOP: Induction: Predose on D1 of Cy2,3,5,6 (1 Cy: 21 days); Maintenance: Predose on D1 of Month 1,2,4,7,15,23; at 120 days and 1 year of last atezolizumab dose or at treatment discontinuation (up to 4 years); Atezo-R-CHOP: Predose on D1 of Cy 2,3,5,8,16,25 (1 Cy: 21 days); at 120 days and 1 year of last atezolizumab dose or at treatment discontinuation (up to 4 years). Predose time point was "any time prior to dose" for Cycles 2,3,5,6,8 during induction phase, for Cycles 16,25 during consolidation treatment, and for Months 1 to 24 during maintenance phase. Atezo-G-Benda: Induction: Predose on D1 of Cy2,3,5,6 (1Cy: 28 days), Cy3D15: Predose; ; Maintenance: Predose on D1 of Month 1,4,7,15,23; at 120 days and 1 year of last atezolizumab dose or at treatment discontinuation (up to 4 years). The percentage of participants with positive results for ATAs to atezolizumab at baseline and at post-baseline time points are reported.

End point type	Secondary

End point timeframe:

Baseline up to approximately 4 years

End point values	Atezo-G-Benda Cohort (Safety Run-In and Expansion Phases)	Atezo-G-CHOP Cohort (Safety Run-In Phase)	Atezo-R-CHOP Cohort (Expansion Phase)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	42	7	42	
Units: percentage of participants				
number (not applicable)				
Baseline (n=42, 7, 35)	2.4	0	14.3	
Induction Cycle 2 Day 1 (n=41, 7, 39)	0	0	2.6	
Consolidation Cycle 16 (n=0, 0, 17)	9999	9999	5.9	
Atezolizumab Day 120 Follow up (n=17, 2, 11)	0	0	9.1	
Atezo PK and Immuno. Follow Up (1YR) (n=12, 4, 18)	0	0	5.6	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to approximately 4 years

Adverse event reporting additional description:

The safety population is defined as all patients who received at least one dose of the study medication.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	Atezo-G-Benda (Safety Run-In and Expansion Phases)

Reporting group description:

Safety run-in phase: Participants with previously untreated or relapsed or refractory FL received obinutuzumab (G) and bendamustine during Cycle 1 (28-day cycle) and atezolizumab, obinutuzumab, and bendamustine during Cycles 2-6, during induction treatment, followed by atezolizumab (once monthly) and obinutuzumab (every other month [q2m]) for 24 months, during maintenance treatment. Expansion phase: Participants with previously untreated FL received same treatment regimen as described for safety run-in phase.

Reporting group title	Atezo-G-CHOP (Safety Run-In Phase)

Reporting group description:

Safety run-in phase: Participants with previously untreated or relapsed or refractory FL received obinutuzumab and CHOP during Cycle 1 (21-day cycle) and atezolizumab, obinutuzumab, and CHOP during Cycles 2-6, during induction treatment, followed by atezolizumab (once monthly) and obinutuzumab (q2m) for 24 months, during maintenance treatment.

Reporting group title	Atezo-R-CHOP (Expansion Phase)

Reporting group description:

Participants with previously untreated DLBCL received rituximab and CHOP during Cycle 1 (21-day cycle) and atezolizumab, rituximab, and CHOP during Cycles 2-8 (atezolizumab and rituximab for 8 cycles and CHOP for either 6 or 8 cycles, as determined by the investigator), during induction treatment, followed by atezolizumab from Cycles 9-25 during consolidation treatment.

Serious adverse events	Atezo-G-Benda (Safety Run-In and Expansion Phases)	Atezo-G-CHOP (Safety Run-In Phase)	Atezo-R-CHOP (Expansion Phase)
Total subjects affected by serious adverse events			
subjects affected / exposed	19 / 42 (45.24%)	2 / 7 (28.57%)	18 / 42 (42.86%)
number of deaths (all causes)	5	1	5
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
ADENOCARCINOMA			
subjects affected / exposed	1 / 42 (2.38%)	0 / 7 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
ADENOCARCINOMA OF COLON			

subjects affected / exposed	1 / 42 (2.38%)	0 / 7 (0.00%)	0 / 42 (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
COLON CANCER			
subjects affected / exposed	1 / 42 (2.38%)	0 / 7 (0.00%)	0 / 42 (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	3 / 42 (7.14%)	0 / 7 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SUDDEN DEATH			
subjects affected / exposed	1 / 42 (2.38%)	0 / 7 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
DYSPNOEA			
subjects affected / exposed	1 / 42 (2.38%)	0 / 7 (0.00%)	0 / 42 (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
LARYNGEAL INFLAMMATION			
subjects affected / exposed	0 / 42 (0.00%)	0 / 7 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
OBLITERATIVE BRONCHIOLITIS			
subjects affected / exposed	1 / 42 (2.38%)	0 / 7 (0.00%)	0 / 42 (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
PULMONARY EMBOLISM			
subjects affected / exposed	1 / 42 (2.38%)	0 / 7 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Injury, poisoning and procedural complications			
INFUSION RELATED REACTION			
subjects affected / exposed	2 / 42 (4.76%)	0 / 7 (0.00%)	0 / 42 (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
Cardiac disorders			
ATRIAL FIBRILLATION			
subjects affected / exposed	0 / 42 (0.00%)	0 / 7 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ATRIAL TACHYCARDIA			
subjects affected / exposed	1 / 42 (2.38%)	0 / 7 (0.00%)	0 / 42 (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 ARREST			
subjects affected / exposed	1 / 42 (2.38%)	0 / 7 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
MYOCARDITIS			
subjects affected / exposed	1 / 42 (2.38%)	0 / 7 (0.00%)	0 / 42 (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
Nervous system disorders			
MIGRAINE			
subjects affected / exposed	1 / 42 (2.38%)	0 / 7 (0.00%)	0 / 42 (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
SYNCOPE			
subjects affected / exposed	1 / 42 (2.38%)	0 / 7 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
AUTOIMMUNE HAEMOLYTIC ANAEMIA			

subjects affected / exposed	0 / 42 (0.00%)	0 / 7 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FEBRILE NEUTROPENIA			
subjects affected / exposed	4 / 42 (9.52%)	1 / 7 (14.29%)	6 / 42 (14.29%)
occurrences causally related to treatment / all	3 / 4	1 / 1	7 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NEUTROPENIA			
subjects affected / exposed	0 / 42 (0.00%)	1 / 7 (14.29%)	0 / 42 (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
THROMBOCYTOPENIA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 7 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
HYPOACUSIS			
subjects affected / exposed	1 / 42 (2.38%)	0 / 7 (0.00%)	0 / 42 (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
Eye disorders			
DIPLOPIA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 7 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	0 / 42 (0.00%)	0 / 7 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
IMMUNE-MEDIATED ENTEROCOLITIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 7 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

INTESTINAL OBSTRUCTION			
subjects affected / exposed	0 / 42 (0.00%)	0 / 7 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NAUSEA			
subjects affected / exposed	1 / 42 (2.38%)	0 / 7 (0.00%)	0 / 42 (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
PANCREATITIS			
subjects affected / exposed	1 / 42 (2.38%)	0 / 7 (0.00%)	0 / 42 (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
SMALL INTESTINAL OBSTRUCTION			
subjects affected / exposed	1 / 42 (2.38%)	0 / 7 (0.00%)	0 / 42 (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
Hepatobiliary disorders			
CHOLECYSTITIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 7 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
ACUTE KIDNEY INJURY			
subjects affected / exposed	1 / 42 (2.38%)	0 / 7 (0.00%)	0 / 42 (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
Infections and infestations			
DIVERTICULITIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 7 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EPSTEIN-BARR VIRUS INFECTION			

subjects affected / exposed	0 / 42 (0.00%)	0 / 7 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROENTERITIS SALMONELLA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 7 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
KIDNEY INFECTION			
subjects affected / exposed	0 / 42 (0.00%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA			
subjects affected / exposed	5 / 42 (11.90%)	0 / 7 (0.00%)	2 / 42 (4.76%)
occurrences causally related to treatment / all	2 / 5	0 / 0	1 / 2
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
PNEUMONIA INFLUENZAL			
subjects affected / exposed	0 / 42 (0.00%)	0 / 7 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA VIRAL			
subjects affected / exposed	1 / 42 (2.38%)	0 / 7 (0.00%)	0 / 42 (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
PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY			
subjects affected / exposed	1 / 42 (2.38%)	0 / 7 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	1 / 1	0 / 0	1 / 1
SEPSIS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 7 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SINUSITIS			

subjects affected / exposed	0 / 42 (0.00%)	0 / 7 (0.00%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SKIN INFECTION			
subjects affected / exposed	1 / 42 (2.38%)	0 / 7 (0.00%)	0 / 42 (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
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	2 / 42 (4.76%)	0 / 7 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY TRACT INFECTION			
subjects affected / exposed	1 / 42 (2.38%)	0 / 7 (0.00%)	0 / 42 (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
URINARY TRACT INFECTION STAPHYLOCOCCAL			
subjects affected / exposed	1 / 42 (2.38%)	0 / 7 (0.00%)	0 / 42 (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

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

Non-serious adverse events	Atezo-G-Benda (Safety Run-In and Expansion Phases)	Atezo-G-CHOP (Safety Run-In Phase)	Atezo-R-CHOP (Expansion Phase)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	42 / 42 (100.00%)	7 / 7 (100.00%)	42 / 42 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
ACROCHORDON			
subjects affected / exposed	0 / 42 (0.00%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
NEOPLASM			
subjects affected / exposed	0 / 42 (0.00%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	0	1	0

OVARIAN EPITHELIAL CANCER			
subjects affected / exposed	0 / 42 (0.00%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	6 / 42 (14.29%)	0 / 7 (0.00%)	1 / 42 (2.38%)
occurrences (all)	9	0	1
PERIPHERAL COLDNESS			
subjects affected / exposed	0 / 42 (0.00%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	3 / 42 (7.14%)	0 / 7 (0.00%)	2 / 42 (4.76%)
occurrences (all)	5	0	4
CHEST DISCOMFORT			
subjects affected / exposed	2 / 42 (4.76%)	1 / 7 (14.29%)	2 / 42 (4.76%)
occurrences (all)	2	1	2
CHEST PAIN			
subjects affected / exposed	10 / 42 (23.81%)	1 / 7 (14.29%)	4 / 42 (9.52%)
occurrences (all)	10	1	4
CHILLS			
subjects affected / exposed	3 / 42 (7.14%)	0 / 7 (0.00%)	1 / 42 (2.38%)
occurrences (all)	5	0	1
FATIGUE			
subjects affected / exposed	23 / 42 (54.76%)	5 / 7 (71.43%)	17 / 42 (40.48%)
occurrences (all)	27	6	22
FEELING COLD			
subjects affected / exposed	0 / 42 (0.00%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
INFLUENZA LIKE ILLNESS			
subjects affected / exposed	7 / 42 (16.67%)	1 / 7 (14.29%)	1 / 42 (2.38%)
occurrences (all)	9	1	1
MUCOSAL INFLAMMATION			
subjects affected / exposed	1 / 42 (2.38%)	2 / 7 (28.57%)	3 / 42 (7.14%)
occurrences (all)	2	3	5
OEDEMA PERIPHERAL			

subjects affected / exposed	3 / 42 (7.14%)	1 / 7 (14.29%)	3 / 42 (7.14%)
occurrences (all)	3	1	4
PAIN			
subjects affected / exposed	2 / 42 (4.76%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	2	1	0
PERIPHERAL SWELLING			
subjects affected / exposed	3 / 42 (7.14%)	1 / 7 (14.29%)	1 / 42 (2.38%)
occurrences (all)	3	2	1
PYREXIA			
subjects affected / exposed	10 / 42 (23.81%)	0 / 7 (0.00%)	5 / 42 (11.90%)
occurrences (all)	12	0	9
Immune system disorders			
SEASONAL ALLERGY			
subjects affected / exposed	3 / 42 (7.14%)	0 / 7 (0.00%)	2 / 42 (4.76%)
occurrences (all)	5	0	2
Reproductive system and breast disorders			
VAGINAL DISCHARGE			
subjects affected / exposed	2 / 42 (4.76%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	2	1	0
VAGINAL HAEMORRHAGE			
subjects affected / exposed	0 / 42 (0.00%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	0	2	0
VULVOVAGINAL PAIN			
subjects affected / exposed	3 / 42 (7.14%)	0 / 7 (0.00%)	0 / 42 (0.00%)
occurrences (all)	3	0	0
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	25 / 42 (59.52%)	5 / 7 (71.43%)	12 / 42 (28.57%)
occurrences (all)	31	9	18
DYSPHONIA			
subjects affected / exposed	3 / 42 (7.14%)	0 / 7 (0.00%)	2 / 42 (4.76%)
occurrences (all)	3	0	2
DYSPNOEA			
subjects affected / exposed	7 / 42 (16.67%)	1 / 7 (14.29%)	3 / 42 (7.14%)
occurrences (all)	8	1	4
EPISTAXIS			

subjects affected / exposed	3 / 42 (7.14%)	0 / 7 (0.00%)	2 / 42 (4.76%)
occurrences (all)	3	0	2
HICCUPS			
subjects affected / exposed	0 / 42 (0.00%)	0 / 7 (0.00%)	3 / 42 (7.14%)
occurrences (all)	0	0	3
NASAL CONGESTION			
subjects affected / exposed	8 / 42 (19.05%)	0 / 7 (0.00%)	3 / 42 (7.14%)
occurrences (all)	8	0	3
OROPHARYNGEAL PAIN			
subjects affected / exposed	8 / 42 (19.05%)	1 / 7 (14.29%)	4 / 42 (9.52%)
occurrences (all)	11	1	4
PHARYNGEAL DISORDER			
subjects affected / exposed	0 / 42 (0.00%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
PRODUCTIVE COUGH			
subjects affected / exposed	4 / 42 (9.52%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	4	1	0
RHINITIS ALLERGIC			
subjects affected / exposed	3 / 42 (7.14%)	1 / 7 (14.29%)	3 / 42 (7.14%)
occurrences (all)	3	1	3
RHINORRHOEA			
subjects affected / exposed	3 / 42 (7.14%)	2 / 7 (28.57%)	5 / 42 (11.90%)
occurrences (all)	3	2	6
SINUS CONGESTION			
subjects affected / exposed	1 / 42 (2.38%)	1 / 7 (14.29%)	2 / 42 (4.76%)
occurrences (all)	1	1	2
UPPER-AIRWAY COUGH SYNDROME			
subjects affected / exposed	1 / 42 (2.38%)	0 / 7 (0.00%)	3 / 42 (7.14%)
occurrences (all)	1	0	4
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	7 / 42 (16.67%)	0 / 7 (0.00%)	3 / 42 (7.14%)
occurrences (all)	7	0	6
INSOMNIA			
subjects affected / exposed	7 / 42 (16.67%)	2 / 7 (28.57%)	7 / 42 (16.67%)
occurrences (all)	7	2	8

MANIA			
subjects affected / exposed	0 / 42 (0.00%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
Product issues			
DEVICE OCCLUSION			
subjects affected / exposed	0 / 42 (0.00%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
Investigations			
AMYLASE INCREASED			
subjects affected / exposed	4 / 42 (9.52%)	0 / 7 (0.00%)	3 / 42 (7.14%)
occurrences (all)	4	0	3
LIPASE INCREASED			
subjects affected / exposed	13 / 42 (30.95%)	1 / 7 (14.29%)	4 / 42 (9.52%)
occurrences (all)	14	1	6
WEIGHT DECREASED			
subjects affected / exposed	1 / 42 (2.38%)	0 / 7 (0.00%)	3 / 42 (7.14%)
occurrences (all)	1	0	3
Injury, poisoning and procedural complications			
FALL			
subjects affected / exposed	1 / 42 (2.38%)	1 / 7 (14.29%)	3 / 42 (7.14%)
occurrences (all)	1	1	5
INFUSION RELATED REACTION			
subjects affected / exposed	29 / 42 (69.05%)	2 / 7 (28.57%)	16 / 42 (38.10%)
occurrences (all)	45	2	16
JOINT DISLOCATION			
subjects affected / exposed	0 / 42 (0.00%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
LIGAMENT SPRAIN			
subjects affected / exposed	0 / 42 (0.00%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	0	2	0
MENISCUS INJURY			
subjects affected / exposed	0 / 42 (0.00%)	2 / 7 (28.57%)	0 / 42 (0.00%)
occurrences (all)	0	2	0
POST PROCEDURAL HAEMATURIA			
subjects affected / exposed	0 / 42 (0.00%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	0	1	0

PROCEDURAL PAIN			
subjects affected / exposed	2 / 42 (4.76%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	3	1	0
SKIN LACERATION			
subjects affected / exposed	2 / 42 (4.76%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	2	1	0
Cardiac disorders			
BRADYCARDIA			
subjects affected / exposed	0 / 42 (0.00%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
PALPITATIONS			
subjects affected / exposed	2 / 42 (4.76%)	2 / 7 (28.57%)	1 / 42 (2.38%)
occurrences (all)	2	2	1
Nervous system disorders			
AMNESIA			
subjects affected / exposed	1 / 42 (2.38%)	1 / 7 (14.29%)	1 / 42 (2.38%)
occurrences (all)	1	1	2
BALANCE DISORDER			
subjects affected / exposed	0 / 42 (0.00%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
DIZZINESS			
subjects affected / exposed	7 / 42 (16.67%)	1 / 7 (14.29%)	4 / 42 (9.52%)
occurrences (all)	12	1	6
DYSGEUSIA			
subjects affected / exposed	0 / 42 (0.00%)	0 / 7 (0.00%)	6 / 42 (14.29%)
occurrences (all)	0	0	6
HEADACHE			
subjects affected / exposed	19 / 42 (45.24%)	1 / 7 (14.29%)	8 / 42 (19.05%)
occurrences (all)	25	1	13
HYPOAESTHESIA			
subjects affected / exposed	4 / 42 (9.52%)	2 / 7 (28.57%)	1 / 42 (2.38%)
occurrences (all)	4	3	1
PARAESTHESIA			
subjects affected / exposed	3 / 42 (7.14%)	0 / 7 (0.00%)	3 / 42 (7.14%)
occurrences (all)	5	0	3
PERIPHERAL SENSORY NEUROPATHY			

subjects affected / exposed	3 / 42 (7.14%)	2 / 7 (28.57%)	13 / 42 (30.95%)
occurrences (all)	3	3	15
TASTE DISORDER			
subjects affected / exposed	2 / 42 (4.76%)	0 / 7 (0.00%)	3 / 42 (7.14%)
occurrences (all)	2	0	3
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	4 / 42 (9.52%)	0 / 7 (0.00%)	6 / 42 (14.29%)
occurrences (all)	4	0	8
IRON DEFICIENCY ANAEMIA			
subjects affected / exposed	0 / 42 (0.00%)	1 / 7 (14.29%)	1 / 42 (2.38%)
occurrences (all)	0	1	1
LYMPH NODE PAIN			
subjects affected / exposed	1 / 42 (2.38%)	1 / 7 (14.29%)	1 / 42 (2.38%)
occurrences (all)	1	1	1
NEUTROPENIA			
subjects affected / exposed	14 / 42 (33.33%)	3 / 7 (42.86%)	22 / 42 (52.38%)
occurrences (all)	22	6	31
THROMBOCYTOPENIA			
subjects affected / exposed	4 / 42 (9.52%)	0 / 7 (0.00%)	1 / 42 (2.38%)
occurrences (all)	6	0	1
Eye disorders			
DRY EYE			
subjects affected / exposed	2 / 42 (4.76%)	2 / 7 (28.57%)	3 / 42 (7.14%)
occurrences (all)	2	2	3
OCULAR HYPERAEMIA			
subjects affected / exposed	1 / 42 (2.38%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	1	1	0
PHOTOPHOBIA			
subjects affected / exposed	0 / 42 (0.00%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
VISION BLURRED			
subjects affected / exposed	3 / 42 (7.14%)	0 / 7 (0.00%)	1 / 42 (2.38%)
occurrences (all)	3	0	1
Gastrointestinal disorders			

ABDOMINAL DISCOMFORT			
subjects affected / exposed	4 / 42 (9.52%)	0 / 7 (0.00%)	0 / 42 (0.00%)
occurrences (all)	4	0	0
ABDOMINAL PAIN			
subjects affected / exposed	8 / 42 (19.05%)	2 / 7 (28.57%)	5 / 42 (11.90%)
occurrences (all)	10	3	5
ABDOMINAL PAIN UPPER			
subjects affected / exposed	6 / 42 (14.29%)	0 / 7 (0.00%)	4 / 42 (9.52%)
occurrences (all)	7	0	4
ASCITES			
subjects affected / exposed	0 / 42 (0.00%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
COLITIS			
subjects affected / exposed	4 / 42 (9.52%)	0 / 7 (0.00%)	0 / 42 (0.00%)
occurrences (all)	4	0	0
CONSTIPATION			
subjects affected / exposed	18 / 42 (42.86%)	3 / 7 (42.86%)	18 / 42 (42.86%)
occurrences (all)	27	4	26
DEFAECATION URGENCY			
subjects affected / exposed	0 / 42 (0.00%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
DIARRHOEA			
subjects affected / exposed	20 / 42 (47.62%)	3 / 7 (42.86%)	14 / 42 (33.33%)
occurrences (all)	47	10	23
DRY MOUTH			
subjects affected / exposed	5 / 42 (11.90%)	0 / 7 (0.00%)	4 / 42 (9.52%)
occurrences (all)	5	0	4
DUODENAL ULCER HAEMORRHAGE			
subjects affected / exposed	0 / 42 (0.00%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
DYSPEPSIA			
subjects affected / exposed	8 / 42 (19.05%)	1 / 7 (14.29%)	2 / 42 (4.76%)
occurrences (all)	11	1	3
FLATULENCE			
subjects affected / exposed	3 / 42 (7.14%)	0 / 7 (0.00%)	0 / 42 (0.00%)
occurrences (all)	4	0	0

GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	3 / 42 (7.14%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	3	1	0
GLOSSITIS			
subjects affected / exposed	1 / 42 (2.38%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	1	1	0
HAEMATOCHEZIA			
subjects affected / exposed	1 / 42 (2.38%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	1	1	0
HAEMORRHOIDAL HAEMORRHAGE			
subjects affected / exposed	0 / 42 (0.00%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
NAUSEA			
subjects affected / exposed	22 / 42 (52.38%)	5 / 7 (71.43%)	13 / 42 (30.95%)
occurrences (all)	42	8	22
RECTAL DISCHARGE			
subjects affected / exposed	0 / 42 (0.00%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
STEATORRHOEA			
subjects affected / exposed	0 / 42 (0.00%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
STOMATITIS			
subjects affected / exposed	3 / 42 (7.14%)	0 / 7 (0.00%)	3 / 42 (7.14%)
occurrences (all)	3	0	5
VOMITING			
subjects affected / exposed	11 / 42 (26.19%)	2 / 7 (28.57%)	9 / 42 (21.43%)
occurrences (all)	15	3	11
Hepatobiliary disorders			
CHOLELITHIASIS			
subjects affected / exposed	0 / 42 (0.00%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
ALOPECIA			
subjects affected / exposed	3 / 42 (7.14%)	2 / 7 (28.57%)	10 / 42 (23.81%)
occurrences (all)	4	2	10
DERMATITIS ACNEIFORM			

subjects affected / exposed	1 / 42 (2.38%)	1 / 7 (14.29%)	2 / 42 (4.76%)
occurrences (all)	1	1	2
DERMATITIS CONTACT			
subjects affected / exposed	0 / 42 (0.00%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	0	2	0
DRY SKIN			
subjects affected / exposed	4 / 42 (9.52%)	1 / 7 (14.29%)	1 / 42 (2.38%)
occurrences (all)	4	1	1
ERYTHEMA			
subjects affected / exposed	4 / 42 (9.52%)	0 / 7 (0.00%)	0 / 42 (0.00%)
occurrences (all)	5	0	0
NIGHT SWEATS			
subjects affected / exposed	4 / 42 (9.52%)	0 / 7 (0.00%)	3 / 42 (7.14%)
occurrences (all)	4	0	3
PRURITUS			
subjects affected / exposed	12 / 42 (28.57%)	0 / 7 (0.00%)	4 / 42 (9.52%)
occurrences (all)	14	0	4
RASH			
subjects affected / exposed	14 / 42 (33.33%)	0 / 7 (0.00%)	4 / 42 (9.52%)
occurrences (all)	22	0	6
RASH MACULO-PAPULAR			
subjects affected / exposed	4 / 42 (9.52%)	0 / 7 (0.00%)	0 / 42 (0.00%)
occurrences (all)	5	0	0
RASH VESICULAR			
subjects affected / exposed	0 / 42 (0.00%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
DYSURIA			
subjects affected / exposed	1 / 42 (2.38%)	1 / 7 (14.29%)	1 / 42 (2.38%)
occurrences (all)	3	1	1
MICTURITION URGENCY			
subjects affected / exposed	0 / 42 (0.00%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
Endocrine disorders			
HYPOPHYSITIS			

subjects affected / exposed	0 / 42 (0.00%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
HYPOTHYROIDISM			
subjects affected / exposed	1 / 42 (2.38%)	1 / 7 (14.29%)	2 / 42 (4.76%)
occurrences (all)	1	1	2
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	8 / 42 (19.05%)	2 / 7 (28.57%)	9 / 42 (21.43%)
occurrences (all)	10	4	12
BACK PAIN			
subjects affected / exposed	10 / 42 (23.81%)	4 / 7 (57.14%)	8 / 42 (19.05%)
occurrences (all)	10	6	13
BONE PAIN			
subjects affected / exposed	4 / 42 (9.52%)	1 / 7 (14.29%)	4 / 42 (9.52%)
occurrences (all)	6	1	5
FLANK PAIN			
subjects affected / exposed	3 / 42 (7.14%)	0 / 7 (0.00%)	2 / 42 (4.76%)
occurrences (all)	6	0	2
JOINT EFFUSION			
subjects affected / exposed	0 / 42 (0.00%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
JOINT SWELLING			
subjects affected / exposed	0 / 42 (0.00%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
MUSCLE SPASMS			
subjects affected / exposed	5 / 42 (11.90%)	2 / 7 (28.57%)	0 / 42 (0.00%)
occurrences (all)	7	2	0
MUSCULOSKELETAL CHEST PAIN			
subjects affected / exposed	2 / 42 (4.76%)	1 / 7 (14.29%)	4 / 42 (9.52%)
occurrences (all)	5	1	4
MUSCULOSKELETAL PAIN			
subjects affected / exposed	4 / 42 (9.52%)	1 / 7 (14.29%)	2 / 42 (4.76%)
occurrences (all)	4	1	2
MUSCULOSKELETAL STIFFNESS			

subjects affected / exposed	1 / 42 (2.38%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	1	1	0
MYALGIA			
subjects affected / exposed	2 / 42 (4.76%)	1 / 7 (14.29%)	5 / 42 (11.90%)
occurrences (all)	3	1	5
NECK PAIN			
subjects affected / exposed	4 / 42 (9.52%)	0 / 7 (0.00%)	2 / 42 (4.76%)
occurrences (all)	4	0	2
PAIN IN EXTREMITY			
subjects affected / exposed	8 / 42 (19.05%)	1 / 7 (14.29%)	2 / 42 (4.76%)
occurrences (all)	10	1	2
Infections and infestations			
BRONCHITIS			
subjects affected / exposed	4 / 42 (9.52%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	4	2	0
CONJUNCTIVITIS			
subjects affected / exposed	2 / 42 (4.76%)	2 / 7 (28.57%)	0 / 42 (0.00%)
occurrences (all)	2	2	0
HERPES ZOSTER			
subjects affected / exposed	2 / 42 (4.76%)	2 / 7 (28.57%)	1 / 42 (2.38%)
occurrences (all)	2	2	1
NASOPHARYNGITIS			
subjects affected / exposed	5 / 42 (11.90%)	0 / 7 (0.00%)	1 / 42 (2.38%)
occurrences (all)	8	0	1
ORAL CANDIDIASIS			
subjects affected / exposed	2 / 42 (4.76%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	2	2	0
ORAL HERPES			
subjects affected / exposed	0 / 42 (0.00%)	1 / 7 (14.29%)	1 / 42 (2.38%)
occurrences (all)	0	1	1
PHARYNGITIS STREPTOCOCCAL			
subjects affected / exposed	0 / 42 (0.00%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
PNEUMONIA			
subjects affected / exposed	4 / 42 (9.52%)	0 / 7 (0.00%)	2 / 42 (4.76%)
occurrences (all)	4	0	2

SINUSITIS			
subjects affected / exposed	7 / 42 (16.67%)	1 / 7 (14.29%)	5 / 42 (11.90%)
occurrences (all)	7	1	5
SKIN INFECTION			
subjects affected / exposed	2 / 42 (4.76%)	1 / 7 (14.29%)	1 / 42 (2.38%)
occurrences (all)	2	1	1
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	12 / 42 (28.57%)	1 / 7 (14.29%)	7 / 42 (16.67%)
occurrences (all)	22	1	7
URINARY TRACT INFECTION			
subjects affected / exposed	6 / 42 (14.29%)	1 / 7 (14.29%)	1 / 42 (2.38%)
occurrences (all)	8	1	2
VULVOVAGINAL MYCOTIC INFECTION			
subjects affected / exposed	1 / 42 (2.38%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	1	1	0
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	6 / 42 (14.29%)	2 / 7 (28.57%)	1 / 42 (2.38%)
occurrences (all)	6	2	1
DEHYDRATION			
subjects affected / exposed	2 / 42 (4.76%)	2 / 7 (28.57%)	2 / 42 (4.76%)
occurrences (all)	3	2	2
HYPERGLYCAEMIA			
subjects affected / exposed	3 / 42 (7.14%)	0 / 7 (0.00%)	0 / 42 (0.00%)
occurrences (all)	3	0	0
HYPOCALCAEMIA			
subjects affected / exposed	0 / 42 (0.00%)	1 / 7 (14.29%)	0 / 42 (0.00%)
occurrences (all)	0	1	0
HYPOKALAEMIA			
subjects affected / exposed	1 / 42 (2.38%)	0 / 7 (0.00%)	3 / 42 (7.14%)
occurrences (all)	1	0	3

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 October 2015	MPDL3280A was changed to atezolizumab throughout the protocol. The management of gastrointestinal, dermatologic, endocrine, pulmonary toxicity, hepatotoxicity, potential pancreatic or ocular events, and other immune mediated adverse events was updated. Guidance on investigations for the differential diagnosis of Systemic immune activation (SIA) was added. An exclusion criterion was added: "Known history of idiopathic pulmonary fibrosis, organizing pneumonia (e.g., bronchiolitis obliterans), drug induced pneumonitis or evidence of active pneumonitis on screening chest CT scan. History of radiation pneumonitis in the radiation field (fibrosis) was allowed." The exclusion criterion related to infections was clarified as follows: "Active bacterial, viral, fungal, or other infection or any major episode of infection requiring treatment with IV antibiotics within 4 weeks of Day 1 of Cycle 1". The use of receptor activator of nuclear factor kappa-B ligand (RANKL) inhibitor (denosumab) was updated. Clarifications were made on the use of vaccines. The exclusion criterion related to prior treatment in relapse or refractory FL subjects (enrolled in safety run-in) was clarified. The administration sequence of the monoclonal antibodies and bendamustine in the Atezo-G-Benda treatment group was clarified. The administration sequence of the monoclonal antibodies and bendamustine in the Atezo-G-Benda treatment group was clarified.
07 September 2016	Further enrollment into the atezolizumab in combination with obinutuzumab plus cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) treatment group at the end of the safety run-in phase is stopped. In the expansion phase, subjects with previously untreated diffuse large B-cell lymphoma (DLBCL) will receive atezolizumab in combination with rituximab plus CHOP. The rationale for this change is based on results from the Phase III BO21005/GOYA study showing that the addition of obinutuzumab to CHOP chemotherapy in subjects with previously untreated DLBCL did not improve the primary endpoint progression-free survival (PFS) compared with the standard regimen of rituximab plus CHOP chemotherapy. Obinutuzumab exposure data has been updated. Guidance for the administration of atezolizumab on Day 15 for the atezolizumab in combination with obinutuzumab plus bendamustine treatment group has been clarified. Atezolizumab can be given on Day 15 of Cycles 2−6 regardless of cytopenia. The rationale for this update to the guidance is based on the mechanism of action of atezolizumab in conjunction with the available clinical experience showing minimal cytopenic effect of atezolizumab as a single agent, with an incidence of neutropenia of < 0.1%. Pharmacokinetic (PK) sampling schedule has been updated to include the "after atezolizumab infusion" serum atezolizumab PK samples at certain timepoints as well as to clarify the sampling time windows.
26 May 2017	The classification of second malignancies was changed from a selected adverse event to adverse event of special interest to more closely monitor this adverse event. Conditions for resuming study treatment in case of Grade ≥ 3 laboratory abnormalities was clarified. The list of adverse events of special interest for atezolizumab was updated. Language was modified to clarify the induction treatment with atezolizumab and CHOP. "Influenza-like illness" was added as an adverse event of special interest immediately reportable to the Sponsor. The protocol was modified to prohibit use of the term "sudden death" on the Adverse Event eCRF, unless it was combined with the presumed cause of death (e.g., "sudden cardiac death").

22 December 2017	Rationale for Treatment Combination section has been updated with the most recent efficacy and safety results from Study GO29383. Risks Associated with Obinutuzumab) has been updated to reflect recent updates to the Obinutuzumab treatment: Hypersensitivity reactions with delayed onset (e.g., serum sickness) have been added to previous warns related to hypersensitivity with immediate onset. The following observation has been added to warnings related to infections: In FL studies, a high incidence of infections was observed in all phases of the studies, including follow-up, with the highest incidence seen in maintenance. Section 5.1.3 (Risks Associated with Atezolizumab) have been revised to remove detailed presentation of the risks associated with atezolizumab. Section 5.1.7 (Management of Specific Adverse Events) management guidelines for atezolizumab-associated adverse events have been updated.
07 November 2018	Lists of risks for atezolizumab and guidelines for managing participants who experienced atezolizumab-associated adverse events was revised to include nephritis; regular Internal Monitoring Committee assessments would no longer take place as no new safety signals were identified with atezolizumab in combination with obinutuzumab plus CHOP or with atezolizumab in combination with rituximab plus CHOP. Ad hoc meetings could be called at the discretion of the Medical Monitor in case of new safety signals; Language regarding post-trial access was changed allowing particpants still under study treatment to enter an extension study in case there was an early closure of Study BO29563; Medical Monitor information was updated.

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.

Development of the atezolizumab combination treatment was discontinued as there was insufficient evidence regarding the additive efficacy of this therapy.

Notes: