Clinical trial results:
A Randomized, Open Label Study of Ofatumumab and Bendamustine Combination Therapy Compared with Bendamustine Monotherapy in Indolent B-cell Non- Hodgkin's Lymphoma Unresponsive to Rituximab or a Rituximab-Containing Regimen During or Within Six Months of Treatment

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use https://www.novctrd.com/CtrdWeb/home.nov for complete trial results.

Summary

EudraCT number	2008-004177-17
Trial protocol	BE FR DE PL IT GR GB AT SK
Global end of trial date	26 December 2018

Results information

Result version number	v1 (current)
This version publication date	12 January 2020
First version publication date	12 January 2020

Trial information

Trial identification

Sponsor protocol code	COMB157E2301/OMB110918

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01077518
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma, AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma, AG, +41 613241111, novartis.email@novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma, AG, +41 613241111, novartis.email@novartis.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	26 December 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	26 December 2018
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To establish the effectiveness of ofatumumab in combination with bendamustine (Ofa+Benda) in subjects with indolent B-cell Non-Hodgkin's Lymphoma disease refractory to rituximab-containing therapy

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 August 2010
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	Argentina: 5
Country: Number of subjects enrolled	Austria: 9
Country: Number of subjects enrolled	Belgium: 39
Country: Number of subjects enrolled	Canada: 54
Country: Number of subjects enrolled	France: 26
Country: Number of subjects enrolled	Germany: 15
Country: Number of subjects enrolled	United Kingdom: 7
Country: Number of subjects enrolled	Greece: 23
Country: Number of subjects enrolled	Italy: 31
Country: Number of subjects enrolled	Japan: 26
Country: Number of subjects enrolled	Poland: 29
Country: Number of subjects enrolled	Russian Federation: 54
Country: Number of subjects enrolled	Slovakia: 3

Country: Number of subjects enrolled	Ukraine: 9
Country: Number of subjects enrolled	United States: 16
Worldwide total number of subjects	346
EEA total number of subjects	182

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)	195
From 65 to 84 years	149
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

346 (173 randomized to Ofa+benda arm and 173 randomized to benda arm)

Pre-assignment

Screening details:

346 (173 randomized to Ofa+benda arm and 173 randomized to benda arm)

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Ofa + benda (Arm A)

Arm description:

ofatumumab and bendamustine arm. Participants received up to 8 cycles of bendamustine (90 mg/m2) on Days 1,2 every 21 days with 12 doses of ofatumumab (1000 mg, Day 1 q21 days when with bendamustine and every 28 days

Arm type	Experimental
Investigational medicinal product name	Ofatumumab
Investigational medicinal product code	OMB157
Other name	Ofa
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Ofatumumab was a liquid concentrate solution for infusion presented in glass vials containing 50 mL of solution at a concentration of 20 mg/mL to provide 1000 mg per vial. The ofatumumab infusions were prepared in 1000 mL sterile, pyrogen-free 0.9% NaCl to yield a 1 mg/mL ofatumumab concentration infusion.

Investigational medicinal product name	bendamustine
Investigational medicinal product code	
Other name	benda
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intracavernous use

Dosage and administration details:

Bendamustine 100 mg/vial, injection 120 mg/m2 Days 1 and 2, every 21 days

Arm title	Benda (Arm B)

Arm description:

Bendamustine monotherapy. Participants received up to 8 cycles of bendamustine (120 mg/m2 on Days 1, 2 every 21 days

Arm type	Active comparator
Investigational medicinal product name	bendamustine
Investigational medicinal product code	
Other name	benda
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intracavernous use

Dosage and administration details:

Bendamustine 100 mg/vial, injection 120 mg/m2 Days 1 and 2, every 21 days

Number of subjects in period 1	Ofa + benda (Arm A)	Benda (Arm B)
Started	173	173
Completed 5-year follow-up	64 [1]	64 [2]
Completed	95	108
Not completed	78	65
Physician decision	10	11
Consent withdrawn by subject	32	28
Study Terminated by Sponsor	28	22
Lost to follow-up	8	4

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This is correct as these subjects completed the study.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: This is correct as these subjects completed the study.

Baseline characteristics

Reporting groups	
Reporting group title	Ofa + benda (Arm A)
Reporting group description:	
ofatumumab and bendamustine arm. Participants received up to 8 cycles of bendamustine (90 mg/m2) on Days 1,2 every 21 days with 12 doses of ofatumumab (1000 mg, Day 1 q21 days when with bendamustine and every 28 days	
Reporting group title	Benda (Arm B)
Reporting group description:	
Bendamustine monotherapy. Participants received up to 8 cycles of bendamustine (120 mg/m2 on Days 1, 2 every 21 days	

Reporting group values	Ofa + benda (Arm A)	Benda (Arm B)	Total
Number of subjects	173	173	346
Age categorical Units: Subjects			
Adults (18-64 years)	100	95	195
From 65-84 years	72	77	149
85 years and over	1	1	2
Age Continuous Units: years			
arithmetic mean	61.8	62.6	
standard deviation	± 61.0	± 63.0	-
Sex: Female, Male Units: participants			
Female	72	71	143
Male	101	102	203
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	10	6	16
Not Hispanic or Latino	163	167	330
Unknown or Not Reported	0	0	0
FLIPI-1 Score at Screening Units: Subjects			
0 - 2	100	93	193
3 - 5	66	75	141
Missing	7	5	12
Baseline Absolute Lymphocyte Count Units: Subjects			
< LLN	41	41	82
>= LLN	131	131	262
Missing	1	1	2
FcR Gamma 3A Variation Units: Subjects			
The GG	21	18	39
The TG	77	59	136
The TT	61	62	123
Missing	14	34	48

Human Anti-Chimeric Antibodies (HACA) Units: Subjects			
Negative	141	116	257
Positive	21	23	44
Missing	11	34	45

Subject analysis sets

Subject analysis set title	Optional Ofa
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Eligible benda arm participants who were offered optional ofatumumab following disease progression

Reporting group values	Optional Ofa		
Number of subjects	30		
Age categorical Units: Subjects			
Adults (18-64 years)	21		
From 65-84 years	11		
85 years and over	0		
Age Continuous Units: years			
arithmetic mean	17		
standard deviation	±		
Sex: Female, Male Units: participants			
Female			
Male			
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino			
Not Hispanic or Latino			
Unknown or Not Reported			
FLIPI-1 Score at Screening Units: Subjects			
0 - 2			
3 - 5			
Missing			
Baseline Absolute Lymphocyte Count Units: Subjects			
< LLN			
>= LLN			
Missing			
FcR Gamma 3A Variation Units: Subjects			
The GG			
The TG			
The TT			
Missing			
Human Anti-Chimeric Antibodies (HACA) Units: Subjects			

Negative Positive Missing			

End points

End points reporting groups

Reporting group title	Ofa + benda (Arm A)
Reporting group description:	
ofatumumab and bendamustine arm. Participants received up to 8 cycles of bendamustine (90 mg/m2) on Days 1,2 every 21 days with 12 doses of ofatumumab (1000 mg, Day 1 q21 days when with bendamustine and every 28 days	
Reporting group title	Benda (Arm B)
Reporting group description:	
Bendamustine monotherapy. Participants received up to 8 cycles of bendamustine (120 mg/m2 on Days 1, 2 every 21 days	
Subject analysis set title	Optional Ofa
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Eligible benda arm participants who were offered optional ofatumumab following disease progression	

Primary: Progression-free survival (PFS) as assessed by the Independent Review Committee (IRC)

End point title	Progression-free survival (PFS) as assessed by the Independent Review Committee (IRC)
End point description:	
PFS is defined as the time interval between randomization until disease progression or death (due to any cause).	
End point type	Primary
End point timeframe:	
From randomization to the date of first documented disease progression or death due to any cause (67.5 months)	

End point values	Ofa + benda (Arm A)	Benda (Arm B)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173	173		
Units: months				
median (confidence interval 95%)	16.66 (12.81 to 19.68)	13.83 (11.30 to 16.89)		

Statistical analyses

Statistical analysis title	PFS per IRC
Comparison groups	Ofa + benda (Arm A) v Benda (Arm B)
Number of subjects included in analysis	346
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.139
Method	Stratified Log-Rank
Parameter estimate	Stratified Cox propor.hazards regression
Point estimate	0.82

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.62
upper limit	1.07

Secondary: Progression-free survival (PFS) in participants with Follicular Lymphoma (FL) per IRC

End point title	Progression-free survival (PFS) in participants with Follicular Lymphoma (FL) per IRC

End point description:

PFS is defined as the time interval between randomization until disease progression or death (due to any cause).

End point type	Secondary

End point timeframe:

From randomization to the date of first documented disease progression or death due to any cause (67.5 months)

End point values	Ofa + benda (Arm A)	Benda (Arm B)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173	173		
Units: months				
median (confidence interval 95%)	16.62 (11.17 to 20.47)	12.12 (10.94 to 16.62)		

Statistical analyses

Statistical analysis title	PFS for FL per IRC
Comparison groups	Ofa + benda (Arm A) v Benda (Arm B)
Number of subjects included in analysis	346
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1076
Method	Stratified Log-Rank
Parameter estimate	Stratified Cox propor.hazards regression
Point estimate	0.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.55
upper limit	1.06

Secondary: Overall response rate (ORR) in All participants per IRC

End point title	Overall response rate (ORR) in All participants per IRC

End point description:

ORR: Percentage of subjects achieving a complete response (CR) or partial response (PR) from the start of randomization until disease progression or the start of new anti-cancer therapy, including the optional ofatumumab for subjects in Arm B. based on responses from the IRC assessment of best overall response using the Revised Response Criteria for Malignant Lymophoma (RRCML) with response criteria defined as CR, PR, standard disease (SD), progressine disease (PD) or NE

End point type	Secondary

End point timeframe:

From randomization until the 217th PFS event occurred, up to about 67.5 months

End point values	Ofa + benda (Arm A)	Benda (Arm B)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173	173		
Units: Percentage of participants				
number (confidence interval 95%)	73 (66 to 80)	75 (67 to 81)		

Statistical analyses

Statistical analysis title	for All participants
Comparison groups	Ofa + benda (Arm A) v Benda (Arm B)
Number of subjects included in analysis	346
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.8003
Method	Cochran-Mantel-Haenszel

Secondary: Overall response rate (ORR) in participants with FL per IRC

End point title	Overall response rate (ORR) in participants with FL per IRC

End point description:

ORR: Percentage of subjects achieving a complete response (CR) or partial response (PR) from the start of randomization until disease progression or the start of new anti-cancer therapy, including the optional ofatumumab for subjects in Arm B. based on responses from the IRC assessment of best overall response using the Revised Response Criteria for Malignant Lymophoma (RRCML) with response criteria defined as CR, PR, standard disease (SD), progressine disease (PD) or NE

End point type	Secondary

End point timeframe:

From randomization until the 217th PFS event occurred, up to about 67.5 months

End point values	Ofa + benda (Arm A)	Benda (Arm B)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173	173		
Units: Percentage of participants				
number (confidence interval 95%)	77 (68 to 84)	76 (67 to 83)		

Statistical analyses

Statistical analysis title	ORR with FL
Statistical analysis description: for Follicular Lymphoma (FL) participants	
Comparison groups	Ofa + benda (Arm A) v Benda (Arm B)
Number of subjects included in analysis	346
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.613
Method	Cochran-Mantel-Haenszel

Secondary: Overall Survival (OS) in All participants

End point title	Overall Survival (OS) in All participants
End point description: The interval of time between the date of randomization and the date of death due to any cause. For subjects who are alive, time of death will be censored at the date of last contact.	
End point type	Secondary
End point timeframe: From randomization up to about 89 months	

End point values	Ofa + benda (Arm A)	Benda (Arm B)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173	173		
Units: months				
median (confidence interval 95%)	59.76 (46.63 to 999)	58.22 (36.44 to 999)		

Statistical analyses

Statistical analysis title	OS for all patients
Statistical analysis description: for All patients	
Comparison groups	Ofa + benda (Arm A) v Benda (Arm B)

Number of subjects included in analysis	346
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.4046
Method	Stratified Log Rank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.62
upper limit	1.21

Secondary: Overall Survival (OS) in participants with FL

End point title	Overall Survival (OS) in participants with FL

End point description:

The interval of time between the date of randomization and the date of death due to any cause. For subjects who are alive, time of death will be censored at the date of last contact.

End point type	Secondary

End point timeframe:

From randomization up to about 89 months

End point values	Ofa + benda (Arm A)	Benda (Arm B)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173	173		
Units: months				
median (confidence interval 95%)	99 (45.60 to 999)	53.59 (36.44 to 999)		

Statistical analyses

Statistical analysis title	OS for FL patients

Statistical analysis description:

for FL participants

Comparison groups	Ofa + benda (Arm A) v Benda (Arm B)
Number of subjects included in analysis	346
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3768
Method	Stratified Log Rank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.83

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.55
upper limit	1.25

Secondary: Time to response in All participants per IRC

End point title	Time to response in All participants per IRC

End point description:

Time to response = time from randomization to the first response (CR/ PR). If no CR/PR value was present data was to be censored at last adequate assessment.

End point type	Secondary

End point timeframe:

From randomization to up to 67.5 months

End point values	Ofa + benda (Arm A)	Benda (Arm B)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173	173		
Units: Months				
median (confidence interval 95%)	2.86 (2.83 to 2.92)	2.89 (2.83 to 2.92)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to response in participants with FL per IRC

End point title	Time to response in participants with FL per IRC

End point description:

Time to response = time from randomization to the first response (CR/ PR). If no CR/PR value was present data was to be censored at last adequate assessment.

End point type	Secondary

End point timeframe:

From randomization to up to 67.5 months

End point values	Ofa + benda (Arm A)	Benda (Arm B)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173	173		
Units: Months				
median (confidence interval 95%)	2.86 (2.83 to 2.92)	2.86 (2.83 to 2.89)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of response in All participants per IRC

End point title	Duration of response in All participants per IRC

End point description:

Time (in months) from the initial response (CR/PR) to first documented sign of disease progression or death due to any cause.

End point type	Secondary

End point timeframe:

time from the initial response (CR/PR) (Day 84) to first documented sign of disease progression or death due to any cause up to 67.5 months

End point values	Ofa + benda (Arm A)	Benda (Arm B)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173	173		
Units: months				
median (confidence interval 95%)	17.71 (13.04 to 22.57)	14.49 (10.84 to 16.76)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of response in participants with FL per IRC

End point title	Duration of response in participants with FL per IRC

End point description:

Time (in months) from the initial response (CR/PR) to first documented sign of disease progression or death due to any cause.

End point type	Secondary

End point timeframe:

time from the initial response (CR/PR) (Day 84) to first documented sign of disease progression or death due to any cause up to 67.5 months

End point values	Ofa + benda (Arm A)	Benda (Arm B)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173	173		
Units: months				
median (confidence interval 95%)	16.39 (11.53 to 20.53)	11.20 (8.61 to 16.43)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to progression in All participants per IRC

End point title	Time to progression in All participants per IRC

End point description:

Time from randomization until disease progression

End point type	Secondary

End point timeframe:

From randomization to the date of first documented disease progression, whichever occurred first, reported betwen day of first participant randomized up to about 67.5 months

End point values	Ofa + benda (Arm A)	Benda (Arm B)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173	173		
Units: Months				
median (confidence interval 95%)	19.35 (14.32 to 23.10)	16.56 (13.63 to 19.75)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to progression in participants with FL per IRC

End point title	Time to progression in participants with FL per IRC

End point description:

Time from randomization until disease progression

End point type	Secondary

End point timeframe:

From randomization to the date of first documented disease progression, whichever occurred first, reported betwen day of first participant randomized up to about 67.5 months

End point values	Ofa + benda (Arm A)	Benda (Arm B)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173	173		
Units: Months				
median (confidence interval 95%)	19.35 (14.16 to 24.87)	13.80 (11.14 to 16.85)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to next therapy in All participants per IRC

End point title	Time to next therapy in All participants per IRC

End point description:

Time to next therapy was defined as the time (in months) from randomization date to the date of receiving the next line treatment, including all therapy types.

End point type	Secondary

End point timeframe:

from randomization date to the date of receiving the next line treatment or death, up to 67.5 months

End point values	Ofa + benda (Arm A)	Benda (Arm B)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173	173		
Units: Months				
median (confidence interval 95%)	39.82 (28.81 to 999)	26.94 (21.72 to 39.75)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to next therapy in participants with FL per IRC

End point title	Time to next therapy in participants with FL per IRC

End point description:

Time to next therapy was defined as the time (in months) from randomization date to the date of receiving the next line treatment, including all therapy types

End point type	Secondary

End point timeframe:

from randomization date to the date of receiving the next line treatment or death, up to 67.5 months

End point values	Ofa + benda (Arm A)	Benda (Arm B)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173	173		
Units: Months				
median (confidence interval 95%)	36.96 (23.79 to 999)	25.43 (18.37 to 47.70)		

Statistical analyses

No statistical analyses for this end point

Secondary: PRO - Change from baseline in Health Related Quality of Life (HRQL) measures in All participants: The FACT-Lym

End point title	PRO - Change from baseline in Health Related Quality of Life (HRQL) measures in All participants: The FACT-Lym

End point description:

The Functional Assessment of Cancer Therapy - Lymphoma (FACT-Lym) is intended as a lymphoma specific additional concerns subscale that is designed to supplement the
FACT-G. The subscale consists of 15 items. Subjects respond to the items on a five point Likert scale ranging from 0 'Not at all' to 4 'Very much' and are asked to think back over the past 7 days when responding to each of the items.
C =cycle; D = day

End point type	Secondary

End point timeframe:

administered at the Screening visit and at all post-baseline, up to 67.5 months (presented at particular clinically relevant time points)

End point values	Ofa + benda (Arm A)	Benda (Arm B)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173	173		
Units: scores on a scale				
arithmetic mean (standard deviation)				
Physical well-being score: C5D1(n=126,118)	0.2 (± 4.36)	-2.8 (± 5.54)		
Physical well-being score C11D1(n=104,78)	1.1 (± 4.58)	1.0 (± 4.25)		
Physical well-being score D252 (n=3, 6)	-5.0 (± 9.64)	1.7 (± 9.18)		
Physical well-being score 12M post-D252 (n=67,53)	0.9 (± 5.59)	1.3 (± 4.52)		
Physical well-being score Withdrawal(n=12, 15)	-4.1 (± 6.78)	-1.5 (± 6.61)		
Social/Family well-being score C5D1(n=126,118)	0.2 (± 4.94)	-0.5 (± 5.24)		
Social/Family well-being score C11D1(n=104,78)	-1.2 (± 6.09)	-1.1 (± 6.45)		
Social/Family well-being score D252 (n=3,6)	-1.6 (± 3.24)	-5.4 (± 9.08)		
Soc./Fam. well-being score 12M post-D252(n=67,53)	0.3 (± 5.21)	-1.3 (± 4.81)		

Social/Family well-being score Withdrawal(n=12,15)	0.9 (± 7.69)	0.3 (± 3.53)		
Emotional well-being score C5D1(n=126,118)	1.7 (± 3.97)	0.1 (± 4.10)		
Emotional well-being score C11D1(n=103,78)	1.4 (± 4.12)	0.7 (± 3.90)		
Emotional well-being score D252(n=3,6)	-5.3 (± 2.08)	-2.5 (± 5.89)		
Emotional well-being score 12M post-D252(n=67,53)	1.5 (± 4.45)	0.7 (± 4.15)		
Emotional well-being score Withdrawal(n=12,15)	-2.2 (± 4.80)	-2.3 (± 4.12)		
Functional well-being score C5D1(n=126,118)	0.7 (± 5.08)	-1.5 (± 5.79)		
Functional well-being score C11D1(n=103,78)	1.1 (± 5.62)	-0.6 (± 5.52)		
Functional well-being score D252(n=3, 6)	-4.3 (± 5.69)	-2.2 (± 13.76)		
Functional well-being score 12M post-D252(n=67,53)	1.1 (± 4.82)	0.8 (± 5.55)		
Functional well-being score Withdrawal(n=12,15)	-2.3 (± 4.27)	-1.6 (± 6.47)		
Lymphoma subscale score C5D1(n=126,118)	3.6 (± 7.88)	-1.0 (± 9.65)		
Lymphoma subscale score C11D1(n=104,78)	4.4 (± 8.88)	2.3 (± 6.53)		
Lymphoma subscale score D252(n=3, 6)	-2.3 (± 14.98)	0.7 (± 18.22)		
Lymphoma subscale score 12M post-D252(n=67,53)	3.2 (± 7.77)	2.0 (± 7.71)		
Lymphoma subscale score Withdrawal(n=12,15)	-1.4 (± 6.16)	-1.6 (± 7.65)		
FACT-Lymphoma TOI C1D1(n=126, 118)	4.5 (± 14.64)	-5.3 (± 18.67)		
FACT-Lymphoma TOI C11D1(n=103,78)	6.7 (± 15.84)	2.7 (± 13.24)		
FACT-Lymphoma TOI D252 (n=3, 6)	-11.7 (± 28.75)	0.2 (± 36.56)		
FACT-Lymphoma TOI 12M post-D252 (n=67,53)	5.1 (± 15.94)	4.1 (± 14.62)		
FACT-Lymphoma TOI Withdrawal(n=12,14)	-7.8 (± 14.55)	-4.3 (± 16.77)		
FACT-G Total Score C5D1 (n=126,118)	2.7 (± 12.82)	-4.7 (± 15.26)		
FACT-G Total Score C11D1 (n=103,78)	2.3 (± 13.00)	0.1 (± 14.11)		
FACT-G Total score D252 (n=3, 6)	-16.2 (± 15.71)	-8.4 (± 31.22)		
FACT-G Total Score 12M post-D252(n=67, 53)	3.7 (± 13.75)	1.5 (± 13.44)		
FACT-G Total Score Withdrawal (n=12, 15)	-7.7 (± 11.91)	-5.3 (± 13.10)		
FACT-Lymph. Tot. score C5D1 (n=126,118)	6.3 (± 18.78)	-5.8 (± 23.05)		
FACT-Lymph. Tot. score C11D1 (n=103,78)	6.7 (± 18.95)	2.4 (± 18.73)		
FACT-Lymph. Tot. score D252(n=3, 6)	-18.6 (± 30.50)	-7.7 (± 44.64)		
FACT-Lymph. Tot. score 12M post-D252 (n=67, 53)	6.9 (± 19.78)	3.5 (± 18.77)		
FACT-Lymph. Tot. score Withdrawal (n=12, 14)	-9.1 (± 15.96)	-6.5 (± 18.53)		

Statistical analyses

No statistical analyses for this end point

Secondary: PRO - Change from baseline in Health Related Quality of Life (HRQL) measures in participants with FL: The FACT-Lym

End point title	PRO - Change from baseline in Health Related Quality of Life (HRQL) measures in participants with FL: The FACT-Lym

End point description:

The Functional Assessment of Cancer Therapy - Lymphoma (FACT-Lym) is intended as a lymphoma specific additional concerns subscale that is designed to supplement the
FACT-G. The subscale consists of 15 items. Subjects respond to the items on a five point Likert scale ranging from 0 'Not at all' to 4 'Very much' and are asked to think back over the past 7 days when responding to each of the items.

End point type	Secondary

End point timeframe:

administered at the Screening visit and at all post-baseline, up to 67.5 months (presented at particular clinically relevant time points)

End point values	Ofa + benda (Arm A)	Benda (Arm B)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173	173		
Units: scores on a scale				
arithmetic mean (standard deviation)				
Physical well-being score C5D1(n=87,78)	0.0 (± 4.66)	-3.4 (± 5.87)		
Physical well-being score C11D1(n=72,47)	0.9 (± 4.16)	1.2 (± 4.74)		
Physical well-being score D252 (n=1, 2)	2.0 (± 999)	7.5 (± 17.68)		
Physical well-being score 12M post-D252 (n=48, 30)	0.5 (± 6.15)	1.8 (± 4.37)		
Physical well-being score Withdrawal(n=6,11)	-5.0 (± 7.64)	-0.6 (± 6.31)		
Social/Family well-being score C5D1(n=87,78)	-0.1 (± 4.38)	-0.7 (± 5.48)		
Social/Family well-being score C11D1(n=72,47)	-1.6 (± 5.38)	-1.4 (± 5.61)		
Social/Family well-being score D252 (n=1, 2)	2.0 (± 999)	2.5 (± 3.54)		
Soc./Fam. well-being score 12M post-D252(n=48,30)	0.3 (± 5.35)	-1.9 (± 5.14)		
Social/Family well-being score Withdrawal(n=6,11)	1.1 (± 5.79)	0.6 (± 2.57)		
Emotional well-being score C5D1(n=87,78)	1.8 (± 3.65)	-0.0 (± 4.41)		
Emotional well-being score C11D1(n=72, 47)	1.2 (± 4.30)	0.5 (± 4.10)		

Emotional well-being score D252(n=1,2)	-6.0 (± 999)	-1.0 (± 9.90)		
Emotional well-being score 12M post-D252(n=48,30)	1.5 (± 4.85)	0.6 (± 2.68)		
Emotional well-being score Withdrawal(n=6,11)	-2.3 (± 5.28)	-1.9 (± 4.59)		
Functional well-being score C5D1(n=87, 78)	0.1 (± 4.58)	-1.7 (± 5.74)		
Functional well-being score C11D1(n=72, 47)	0.5 (± 4.99)	-0.0 (± 4.84)		
Functional well-being score D252(n=1, 2)	-6.0 (± 999)	7.0 (± 15.56)		
Functional well-being score 12M post-D252(n=48,30)	0.7 (± 4.99)	1.0 (± 5.75)		
Functional well-being score Withdrawal(6,11)	-1.6 (± 4.06)	-1.5 (± 7.15)		
Lymphoma subscale score C5D1(n=87,78)	3.7 (± 7.33)	-2.2 (± 9.71)		
Lymphoma subscale score C11D1(n=72,47)	3.7 (± 8.70)	2.4 (± 6.79)		
Lymphoma subscale score D252(n=1, 2)	-18.7 (± 999)	7.0 (± 38.18)		
Lymphoma subscale score 12M post-D252(n=48,30)	2.6 (± 8.00)	2.2 (± 6.63)		
Lymphoma subscale score Withdrawal(n=6,11)	-2.5 (± 6.76)	-0.4 (± 7.17)		
FACT-Lymphoma TOI C5D1(n=87,78)	3.7 (± 13.51)	-7.3 (± 18.77)		
FACT-Lymphoma TOI C11D1(n=72,47)	5.0 (± 14.74)	3.6 (± 14.01)		
FACT-Lymphoma TOI D252(n=1, 2)	-2.0 (± 999)	21.5 (± 71.42)		
FACT-Lymphoma TOI 12M post-D252(n=48,30)	3.7 (± 16.94)	4.9 (± 12.32)		
FACT-Lymphoma TOI Withdrawal(n=6, 10)	-9.2 (± 15.40)	-1.7 (± 15.26)		
FACT-G Total score C5D1(n=87,78)	1.7 (± 11.40)	-5.8 (± 16.32)		
FACT-G Total score C11D1(n=72,47)	1.0 (± 12.17)	0.2 (± 13.96)		
FACT-G Total score D252(n=1, 2)	-8.0 (± 999)	16.0 (± 39.60)		
FACT-G Total score 12M post-D252(n=48,30)	2.9 (± 14.62)	1.4 (± 11.25)		
FACT-Lymphoma Tot. score C5D1(n=87,78)	5.4 (± 16.55)	-8.0 (± 24.11)		
FACT-Lymphoma Tot. score C11D1(n=72,47)	4.7 (± 17.52)	2.7 (± 19.60)		
FACT-Lymphoma Tot. score D252(n=1, 2)	-6.0 (± 999)	23.0 (± 77.78)		
FACT-Lymphoma Tot. score 12M post-D252(n=48,30)	5.5 (± 20.73)	3.6 (± 14.44)		
FACT-Lymphoma Tot. score Withdrawal(n=6, 10)	-10.4 (± 15.02)	-3.1 (± 18.48)		

Statistical analyses

No statistical analyses for this end point

Secondary: PRO - Change from baseline in HRQL measures in all participants: The EQ-5D

End point title	PRO - Change from baseline in HRQL measures in all participants: The EQ-5D

End point description:

The EuroQoL Five-Dimension (EQ-5D) is a self-administered, generic, indirect utility measure used for health economic analysis. It consists of a 0-100 Visual Analogue Scale (VAS) on which subjects are asked to rate their current overall health status & 5 single-item dimensions which ask subjects to rate their health in terms of mobility, self-care, usual activities, pain/discomfort and anxiety/depression. The 5 single items can be summed and expressed as a single global index of health-related quality of life. For each of the 5 items subjects must choose between 3 levels of difficulty in accomplishing tasks in that dimension. The VAS is then used in combination with the dimension scores to generate a subject profile. 1 response exists per dimension: Level 1 (no problem) is coded as "1"; Level 2 (some or moderate problems) is coded as "2"; Level 3 (unable, or extreme problems) is coded as "3".

End point type	Secondary

End point timeframe:

administered at the Screening visit and at all post-baseline, up to 67.5 months (presented at particular clinically relevant time points)

End point values	Ofa + benda (Arm A)	Benda (Arm B)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173	173		
Units: scores on a scale				
arithmetic mean (standard deviation)				
EQ5D01-EQ VAS Score C5D1(n=124,115)	5.8 (± 18.10)	-3.8 (± 19.25)		
EQ5D01-EQ VAS Score C11D1(n=101,78)	12.9 (± 19.38)	2.7 (± 18.96)		
EQ5D01-EQ VAS Score D252 (n=3,6)	-11.7 (± 16.07)	-0.8 (± 19.66)		
EQ5D01-EQ VAS Score 12M post-D252(n=65,52)	14.7 (± 19.71)	7.1 (± 19.14)		
EQ5D01-EQ VAS Score Withdrawal (n=12, 15)	-14.7 (± 17.03)	0.7 (± 34.41)		
EuroQoL Tariffs C5D1(n=122,116)	0.21 (± 0.24)	0.0 (± 0.22)		
EuroQoL Tariffs C11D1(n=102,78)	0.1 (± 0.22)	0.0 (± 0.19)		
EuroQoL Tariffs D252 (n=3, 6)	-0.4 (± 0.79)	0.1 (± 0.36)		
EuroQoL Tariffs 12M post-D252(n=65,51)	0.0 (± 0.22)	0.0 (± 0.20)		
EuroQoL Tariffs Withdrawal (n=12,15)	-0.2 (± 0.22)	0.1 (± 0.32)		

Statistical analyses

No statistical analyses for this end point

Secondary: PRO - Change from baseline in HRQL measures in participants with FL: The EQ-5D

End point title	PRO - Change from baseline in HRQL measures in participants with FL: The EQ-5D

End point description:

The EuroQoL Five-Dimension (EQ-5D) is a self-administered, generic, indirect utility measure used for health economic analysis. It consists of a 0-100 Visual Analogue Scale (VAS) on which subjects are asked to rate their current overall health status & 5 single-item dimensions which ask subjects to rate their health in terms of mobility, self-care, usual activities, pain/discomfort and anxiety/depression. The 5 single items can be summed and expressed as a single global index of health-related quality of life. For each of the 5 items subjects must choose between 3 levels of difficulty in accomplishing tasks in that

dimension. The VAS is then used in combination with the dimension scores to generate a subject profile. 1 response exists per dimension: Level 1 (no problem) is coded as "1"; Level 2 (some or moderate problems) is coded as "2"; Level 3 (unable, or extreme problems) is coded as "3".

End point type	Secondary

End point timeframe:

administered at the Screening visit and at all post-baseline, up to 67.5 months (presented at particular clinically relevant time points)

End point values	Ofa + benda (Arm A)	Benda (Arm B)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	120	119		
Units: scores on a scale				
arithmetic mean (standard deviation)				
EQ5D01-EQ VAS Score C5D1(n=85,76)	5.5 (± 19.25)	-6.5 (± 18.83)		
EQ5D01-EQ VAS Score C11D1(n=69,47)	12.9 (± 19.88)	1.1 (± 20.87)		
EQ5D01-EQ VAS Score D252 (n=1,2)	0.00 (± 999)	-7.5 (± 31.82)		
EQ5D01-EQ VAS Score 12M post-D252(n=46,29)	14.2 (± 21.47)	6.7 (± 20.77)		
EQ5D01-EQ VAS Score Withdrawal (n=6,11)	-18.5 (± 13.35)	5.4 (± 37.78)		
EuroQoL Tariffs C5D1(n=84, 76)	0.0 (± 0.24)	0.0 (± 0.23)		
EuroQoL Tariffs C11D1(n=70, 47))	0.1 (± 0.22)	0.0 (± 0.20)		
EuroQoL Tariffs D252 (n=1, 2)	0.0 (± 999)	0.4 (± 0.53)		
EuroQoL Tariffs 12M post-D252(n=46,28)	0.0 (± 0.22)	0.0 (± 0.16)		
EuroQoL Tariffs Withdrawal (n=6,11)	-0.1 (± 0.16)	0.1 (± 0.36)		

Statistical analyses

No statistical analyses for this end point

Secondary: PRO - Change in health treatment in HRQL measures in all participants: The Health Change Questionnaire (HCQ)

End point title	PRO - Change in health treatment in HRQL measures in all participants: The Health Change Questionnaire (HCQ)

End point description:

The Health Change Questionnaire,
(HCQ) used is a nine item scale that asks the patient to rate change in status since beginning treatment on this study. Subject response provides
an ongoing evaluation of perceived progress and satisfaction with treatment services.

End point type	Secondary

End point timeframe:

administered at the Screening visit and at all post-baseline, up to 67.5 months (presented at particular clinically relevant time points)

End point values	Ofa + benda (Arm A)	Benda (Arm B)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173	173		
Units: scores on a scale				
arithmetic mean (standard deviation)				
Change in health treatment C5D1(n=124, 118)	2.8 (± 1.81)	3.8 (± 2.29)		
Change in health treatment C11D1(n=105, 77)	2.6 (± 1.73)	2.5 (± 1.74)		
Change in health treatment D252(n=3, 6)	5.3 (± 2.52)	4.8 (± 2.56)		
Change in health treatment 12M post D252(n=66, 50)	2.4 (± 1.95)	2.6 (± 1.99)		
Change in health treatment Withdrawal (n=11, 15)	5.4 (± 3.32)	4.3 (± 2.63)		

Statistical analyses

No statistical analyses for this end point

Secondary: PRO - Change in health treatment in HRQL measures in participants with FL: The Health Change Questionnaire (HCQ)

End point title	PRO - Change in health treatment in HRQL measures in participants with FL: The Health Change Questionnaire (HCQ)

End point description:

The Health Change Questionnaire,
(HCQ) used is a nine item scale that asks the patient to rate change in status since beginning treatment on this study. Subject response provides
an ongoing evaluation of perceived progress and satisfaction with treatment services.

End point type	Secondary

End point timeframe:

administered at the Screening visit and at all post-baseline, up to 67.5 months (presented at particular clinically relevant time points)

End point values	Ofa + benda (Arm A)	Benda (Arm B)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	120	119		
Units: scores on a scale				
arithmetic mean (standard deviation)				
Change in health treatment C5D1(n=86, 78)	2.9 (± 1.93)	3.9 (± 2.25)		
Change in health treatment C11D1(n=73, 46)	2.7 (± 1.73)	2.4 (± 1.56)		
Change in health treatment D252(n=1, 2)	3.0 (± 999)	4.5 (± 3.54)		
Change in health treatment 12M post D252(n=47,27)	2.7 (± 2.11)	2.1 (± 1.54)		
Change in health treatment Withdrawal (n=5,11)	7.2 (± 1.79)	4.2 (± 2.96)		

Statistical analyses

No statistical analyses for this end point

Secondary: Reduction in tumor size

End point title	Reduction in tumor size

End point description:

Tumor size was measured by the mean change in the sum of the products of the greatest diameter (SPD) of the largest abnormal nodes from baseline to post-baseline by CT Scan.

End point type	Secondary

End point timeframe:

baseline, post-baseline (up to 55 months)

End point values	Ofa + benda (Arm A)	Benda (Arm B)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173	173		
Units: mm^2				
arithmetic mean (standard deviation)	-33.2 (± 44.08)	-32.8 (± 36.83)		

Statistical analyses

No statistical analyses for this end point

Secondary: Improvement in Eastern Cooperative Oncology Group (ECOG) Performance status

End point title	Improvement in Eastern Cooperative Oncology Group (ECOG) Performance status

End point description:

Improvement was defined as decrease from baseline by at least one step on the ECOG performance status scale (improvement categorized as yes or no).

End point type	Secondary

End point timeframe:

from baseline to End of study up to 67.5 months

End point values	Ofa + benda (Arm A)	Benda (Arm B)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173	173		
Units: participants				
C5D1 (n= 142, 134): Deteriorated	18	24		
C5D1 (n= 142, 134): Improved	30	22		
C5D1 (n= 142, 134): No Change	94	88		
C11D1 (n= 115, 90): Deteriorated	13	9		
C11D1 (n= 115, 90): Improved	27	23		
C11D1 (n= 115, 90): No Change	75	58		
12M post D252 (n= 70, 56): Deteriorated	9	6		
12M post-D252 (n= 70, 56): Improved	17	12		
12M post-D252 (n= 70, 56): No Change	44	38		
Withdrawal (n= 17, 21): Deteriorated	7	8		
Withdrawal (n= 17, 21): Improved	2	2		
Withdrawal (n= 17, 21): No Change	8	11		

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of number of participants with Human Anti-Human Antibodies (HAHA)

End point title	Summary of number of participants with Human Anti-Human Antibodies (HAHA)[1]

End point description:

A summary by responders and non-responders

End point type	Secondary

End point timeframe:

From randomization up to about 67.5 months

Notes:

[1] - 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 was planned for this endpoint.

End point values	Ofa + benda (Arm A)			
Subject group type	Reporting group			
Number of subjects analysed	172			
Units: Participants				
with Post-Ofatumumab HAHA results	151			
with at least 1 conf. +ve post-Ofa HAHA result	1			
-ve post-Ofa HAHA results, no Ofa conc. <200 ug/mL	6			
-ve post-Ofa HAHA, at least 1 Ofa conc<200ug/mL	144			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall response rate (ORR) to optional ofatumumab monotherapy in subjects who progressed during or following single-agent bendamustine

End point title	Overall response rate (ORR) to optional ofatumumab monotherapy in subjects who progressed during or following single-agent bendamustine

End point description:

Percentage of subjects achieving a CR or PR from the start of randomization until disease progression or the start of new anti-cancer therapy, including the optional ofatumumab for subjects in Arm B. Based on responses from the IRC assessment of best overall response using the Revised Response Criteria for Malignant Lymophoma (RRCML) with response criteria defined as CR, PR, SD, PD or NE

End point type	Secondary

End point timeframe:

From randomization until the 217th PFS event occurred, up to about 67.8 months

End point values	Optional Ofa			
Subject group type	Subject analysis set			
Number of subjects analysed	30			
Units: Percentage of participants	17			

Statistical analyses

No statistical analyses for this end point

Secondary: Quantitative assessments of immunoglobulins A, G and M (IgA, IgG, IgM)

End point title	Quantitative assessments of immunoglobulins A, G and M (IgA, IgG, IgM)[2]

End point description:

at scheduled visits for actual values as well as for change from baseline

End point type	Secondary

End point timeframe:

prior to receiving ofatumumab, at first monthly dose, and at 1, 3, and 6 months post last infusion of ofatumumab

Notes:

[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 was planned for this endpoint.

End point values	Ofa + benda (Arm A)			
Subject group type	Reporting group			
Number of subjects analysed	173			
Units: g/L				
arithmetic mean (standard deviation)				
IgA @ screening (BL) (n=1)	0.7 (± 999)			
IgG @ screening (n=1)	4.7 (± 999)			
IgM @ screening (n=1)	0.6 (± 999)			
IgA @ C1D1 (n=134)	1.3 (± 0.78)			
IgG @ C1D1 (n=153)	7.7 (± 3.96)			
IgM @ C1D1 (n=120)	1.4 (± 4.15)			
IgA @ 1M post-D252 (n=77)	1.1 (± 0.74)			
IgG @ 1M post-D252 (n=90)	7.1 (± 2.90)			
IgM @ 1M post-D252 (n=50)	0.6 (± 0.68)			
IgA @ 6M post D252 (n=65)	1.1 (± 0.59)			
IgG @ 6M post D252 (n=75)	7.3 (± 2.97)			
IgM @ 6M post D252 (n=41)	0.7 (± 0.97)			
IgA @ 12M post D252 (n=53)	1.1 (± 1.2)			
IgG @12M post D252 (n=63)	7.1 (± 3.31)			
IgM @ 12M post D252 (n=41)	0.7 (± 0.66)			

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma ofatumumab concentrations

End point title	Plasma ofatumumab concentrations[3]

End point description:

Concentrations of ofatumumab in plasma listed by actual relative time and summarized by nominal time.

End point type	Secondary

End point timeframe:

Cycle 1 Day 1 up to 12 months follow up

Notes:

[3] - 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 was planned for this endpoint.

End point values	Ofa + benda (Arm A)			
Subject group type	Reporting group			
Number of subjects analysed	173			
Units: ug/mL				
arithmetic mean (standard deviation)				
C1D1 End of infusion (EOI) (n=64	262.0 (± 83.97)			
C1D1 1h post-EOI (n=61	283.2 (± 227.11)			
C7D1 pre-dose (n=128)	153.6 (± 74.45)			

C7D1 EOI (n=42)	402.2 (± 148.78)			
C7D1 1h post-EOI (n=39)	419.1 (± 167.44)			
C12D1 pre-dose (n=101)	143.5 (± 75.58)			
C12D1 EOI (n=27)	392.0 (± 130.64)			
12M post-D252 (n=43)	0.9 (± 2.53)			
Withdrawal (n=13)	29.6 (± 42.58)			

Statistical analyses

No statistical analyses for this end point

Secondary: Participants with complete B-cell depletion and near-complete B-cell depletion: B-cell monitoring (CD19+, CD20+)

End point title	Participants with complete B-cell depletion and near-complete B-cell depletion: B-cell monitoring (CD19+, CD20+)

End point description:

The percent change of CD5+CD19+ and CD5-CD19+ from baseline was summarized to assess the treatment effect, to monitor the normal B-cell population, and to follow their recovery.

Complete B-cell depletion is defined as the absolute value of CD5+CD19+ and CD5-CD19+ both equal to zero cells/uL.

End point type	Secondary

End point timeframe:

From Baseline up to 18 months follow up

End point values	Ofa + benda (Arm A)	Benda (Arm B)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173	173		
Units: percentage change from baseline				
arithmetic mean (standard deviation)				
C5D1: CD45+CD19+ (n=18, 1)	-94.0 (± 16.6)	-97.0 (± 999)		
1M post-D252: CD45+CD19+ (n=27, 0)	-82.0 (± 77.0)	999 (± 999)		
9M post-D252: CD45+CD19+ (n=15, 0)	1421.0 (± 5721.6)	999 (± 999)		
C1D1: CD45+CD20+ (n=17,1)	-100.0 (± 0.0)	-98.0 (± 999)		
1M post-D252: CD45+CD20+ (n=26, 0)	-100.0 (± 0.0)	999 (± 999)		
9M post-D252: CD45+CD20+ (n=15, 0)	925.0 (± 3803.1)	999 (± 999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Human Anti-chimeric Antibodies (HACA) Over Time

End point title	Human Anti-chimeric Antibodies (HACA) Over Time

End point description:

The percentage of participants with positive and negative baseline HACA results

End point type	Secondary

End point timeframe:

At Baselone and Cycle 1 day 1

End point values	Ofa + benda (Arm A)	Benda (Arm B)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	173	173		
Units: paercentage of participants				
Baseline: Negative (n = 172, 170)	86	70		
Baseline: Positive (n = 172, 170)	13	14		
C1D1: Negative (n=170, 142)	87	84		
C1D1:Positive (n=170, 142)	13	16		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Timeframe for AE	
Adverse event reporting additional description:	
AE additional description	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups	
Reporting group title	Total
Reporting group description:	
Total	
Reporting group title	OFA + BENDA
Reporting group description:	
OFA + BENDA	
Reporting group title	BENDA
Reporting group description:	
BENDA	
Reporting group title	Optional OFA
Reporting group description:	
Optional OFA	

Serious adverse events	Total	OFA + BENDA	BENDA
Total subjects affected by serious adverse events			
subjects affected / exposed	160 / 342 (46.78%)	72 / 172 (41.86%)	84 / 170 (49.41%)
number of deaths (all causes)	137	66	71
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	2 / 342 (0.58%)	1 / 172 (0.58%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Adenocarcinoma gastric			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (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
Adenocarcinoma pancreas			

subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Basal cell carcinoma			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Benign ovarian tumour			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (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
Brain neoplasm			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Burkitt's lymphoma			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (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
Colon cancer metastatic			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diffuse large B-cell lymphoma			
subjects affected / exposed	2 / 342 (0.58%)	1 / 172 (0.58%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Lung adenocarcinoma			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (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
Lung neoplasm malignant			

subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (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
Malignant melanoma			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Myelodysplastic syndrome			
subjects affected / exposed	3 / 342 (0.88%)	2 / 172 (1.16%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	2 / 2	1 / 1
deaths causally related to treatment / all	0 / 2	0 / 1	0 / 1
Myelofibrosis			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Pancreatic carcinoma			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Transitional cell carcinoma			
subjects affected / exposed	2 / 342 (0.58%)	2 / 172 (1.16%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour haemorrhage			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour pain			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Aortic aneurysm			

subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (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
Aortic aneurysm rupture			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Circulatory collapse			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Embolism			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Hypertension			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (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
Jugular vein thrombosis			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (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
Lymphoedema			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (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
Subclavian vein thrombosis			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (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
General disorders and administration site conditions			
Asthenia			

subjects affected / exposed	3 / 342 (0.88%)	1 / 172 (0.58%)	2 / 170 (1.18%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	4 / 342 (1.17%)	3 / 172 (1.74%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 4	0 / 3	0 / 1
Disease progression			
subjects affected / exposed	2 / 342 (0.58%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 1
Fatigue			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	3 / 342 (0.88%)	1 / 172 (0.58%)	2 / 170 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 2
Malaise			
subjects affected / exposed	3 / 342 (0.88%)	1 / 172 (0.58%)	2 / 170 (1.18%)
occurrences causally related to treatment / all	0 / 0	1 / 1	2 / 2
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Mucosal inflammation			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (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
Multiple organ dysfunction syndrome			
subjects affected / exposed	2 / 342 (0.58%)	0 / 172 (0.00%)	2 / 170 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 2
Pyrexia			

subjects affected / exposed	16 / 342 (4.68%)	7 / 172 (4.07%)	9 / 170 (5.29%)
occurrences causally related to treatment / all	0 / 0	4 / 8	6 / 10
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Systemic inflammatory response syndrome			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	2 / 342 (0.58%)	0 / 172 (0.00%)	2 / 170 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Type IV hypersensitivity reaction			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Social circumstances			
Loss of personal independence in daily activities			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchiectasis			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (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
Chronic obstructive pulmonary disease			

subjects affected / exposed	3 / 342 (0.88%)	1 / 172 (0.58%)	2 / 170 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Dyspnoea			
subjects affected / exposed	3 / 342 (0.88%)	1 / 172 (0.58%)	2 / 170 (1.18%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (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
Pleural effusion			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
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 aspiration			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Pneumonitis			
subjects affected / exposed	5 / 342 (1.46%)	1 / 172 (0.58%)	4 / 170 (2.35%)
occurrences causally related to treatment / all	0 / 0	0 / 1	3 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Productive cough			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	4 / 342 (1.17%)	3 / 172 (1.74%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 3	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary oedema			

subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (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
Pulmonary thrombosis			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (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
Respiratory distress			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Psychiatric disorders			
Abnormal behaviour			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Confusional state			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (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
Depression			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (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
Investigations			
Cytomegalovirus test positive			
subjects affected / exposed	2 / 342 (0.58%)	0 / 172 (0.00%)	2 / 170 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutrophil count decreased			

subjects affected / exposed	2 / 342 (0.58%)	2 / 172 (1.16%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oxygen saturation decreased			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (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
Femur fracture			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaw fracture			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (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
Multiple fractures			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (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
Multiple injuries			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			

Acute coronary syndrome			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (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
Cardiac arrest			
subjects affected / exposed	2 / 342 (0.58%)	0 / 172 (0.00%)	2 / 170 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Cardiac failure chronic			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (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
Cardiac failure congestive			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Cardio-respiratory arrest			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Cardiopulmonary failure			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Coronary artery disease			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (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
Left ventricular dysfunction			

subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Sinus tachycardia			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular tachycardia			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (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
Tachycardia			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (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
Ventricular tachycardia			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebral haemorrhage			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Cerebrovascular accident			
subjects affected / exposed	2 / 342 (0.58%)	1 / 172 (0.58%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 2	0 / 1	0 / 1
Generalised tonic-clonic seizure			

subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Lethargy			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paraparesis			
subjects affected / exposed	2 / 342 (0.58%)	2 / 172 (1.16%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Status epilepticus			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (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
Transient ischaemic attack			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular encephalopathy			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	12 / 342 (3.51%)	2 / 172 (1.16%)	10 / 170 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 2	9 / 11
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aplastic anaemia			

subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (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
Autoimmune haemolytic anaemia			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
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	15 / 342 (4.39%)	8 / 172 (4.65%)	5 / 170 (2.94%)
occurrences causally related to treatment / all	0 / 0	8 / 9	6 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemolytic anaemia			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (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
Haemorrhagic anaemia			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Leukopenia			
subjects affected / exposed	4 / 342 (1.17%)	1 / 172 (0.58%)	3 / 170 (1.76%)
occurrences causally related to treatment / all	0 / 0	0 / 1	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	14 / 342 (4.09%)	6 / 172 (3.49%)	8 / 170 (4.71%)
occurrences causally related to treatment / all	0 / 0	8 / 9	9 / 9
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Pancytopenia			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (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	8 / 342 (2.34%)	2 / 172 (1.16%)	6 / 170 (3.53%)
occurrences causally related to treatment / all	0 / 0	2 / 2	5 / 6
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Thrombocytopenic purpura			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Optic atrophy			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal artery occlusion			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal haemorrhage			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
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	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (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
Diarrhoea			
subjects affected / exposed	2 / 342 (0.58%)	1 / 172 (0.58%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal perforation			

subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Faecalith			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (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
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
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	2 / 342 (0.58%)	0 / 172 (0.00%)	2 / 170 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Stomatitis			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	3 / 342 (0.88%)	2 / 172 (1.16%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	1 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Drug-induced liver injury			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatorenal syndrome			

subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Hyperbilirubinaemia			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (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
Portal vein thrombosis			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (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
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paraneoplastic pemphigus			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stevens-Johnson syndrome			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Toxic epidermal necrolysis			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Urticaria			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
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 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Nephrolithiasis			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (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
Renal failure			
subjects affected / exposed	3 / 342 (0.88%)	1 / 172 (0.58%)	2 / 170 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Urinary tract inflammation			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (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
Pathological fracture			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (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
Infections and infestations			
Abdominal sepsis			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Acinetobacter bacteraemia			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0

Atypical pneumonia			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchiolitis			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopulmonary aspergillosis			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Candida infection			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (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
Cellulitis			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile infection			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (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
Cytomegalovirus chorioretinitis			
subjects affected / exposed	2 / 342 (0.58%)	1 / 172 (0.58%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus infection			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related sepsis			

subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysentery			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia urinary tract infection			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile infection			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
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			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (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
Herpes ophthalmic			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	5 / 342 (1.46%)	1 / 172 (0.58%)	4 / 170 (2.35%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster disseminated			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (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
Infective exacerbation of chronic obstructive airways disease			

subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Klebsiella sepsis			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (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
Lower respiratory tract infection			
subjects affected / exposed	2 / 342 (0.58%)	0 / 172 (0.00%)	2 / 170 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Lung infection			
subjects affected / exposed	5 / 342 (1.46%)	3 / 172 (1.74%)	2 / 170 (1.18%)
occurrences causally related to treatment / all	0 / 0	2 / 3	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenic infection			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal candidiasis			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Pharyngitis			

subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumocystis jirovecii infection			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (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
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	3 / 342 (0.88%)	0 / 172 (0.00%)	2 / 170 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Pneumonia			
subjects affected / exposed	25 / 342 (7.31%)	10 / 172 (5.81%)	14 / 170 (8.24%)
occurrences causally related to treatment / all	0 / 0	4 / 10	6 / 15
deaths causally related to treatment / all	0 / 8	0 / 2	0 / 6
Pneumonia cytomegaloviral			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative abscess			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (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
Progressive multifocal leukoencephalopathy			
subjects affected / exposed	2 / 342 (0.58%)	1 / 172 (0.58%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Pulmonary sepsis			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (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
Respiratory tract infection			

subjects affected / exposed	3 / 342 (0.88%)	2 / 172 (1.16%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	3 / 342 (0.88%)	1 / 172 (0.58%)	2 / 170 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Septic shock			
subjects affected / exposed	3 / 342 (0.88%)	1 / 172 (0.58%)	2 / 170 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 2
Sinusitis			
subjects affected / exposed	3 / 342 (0.88%)	1 / 172 (0.58%)	2 / 170 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin infection			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (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
Spinal cord infection			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal sepsis			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (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
Staphylococcal skin infection			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (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
Subcutaneous abscess			

subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tuberculosis			
subjects affected / exposed	2 / 342 (0.58%)	1 / 172 (0.58%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Upper respiratory tract infection			
subjects affected / exposed	2 / 342 (0.58%)	0 / 172 (0.00%)	2 / 170 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	2 / 342 (0.58%)	2 / 172 (1.16%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	2 / 342 (0.58%)	1 / 172 (0.58%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Varicella			
subjects affected / exposed	1 / 342 (0.29%)	1 / 172 (0.58%)	0 / 170 (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
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	3 / 342 (0.88%)	0 / 172 (0.00%)	3 / 170 (1.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes mellitus			

subjects affected / exposed	1 / 342 (0.29%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Failure to thrive			
subjects affected / exposed	2 / 342 (0.58%)	2 / 172 (1.16%)	0 / 170 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Hypokalaemia			
subjects affected / exposed	3 / 342 (0.88%)	0 / 172 (0.00%)	3 / 170 (1.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Optional OFA		
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 32 (25.00%)		
number of deaths (all causes)	15		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	0 / 32 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Adenocarcinoma gastric			
subjects affected / exposed	0 / 32 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Adenocarcinoma pancreas			
subjects affected / exposed	0 / 32 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Basal cell carcinoma			
subjects affected / exposed	0 / 32 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Benign ovarian tumour				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Brain neoplasm				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Burkitt's lymphoma				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Colon cancer metastatic				
subjects affected / exposed	1 / 32 (3.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diffuse large B-cell lymphoma				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lung adenocarcinoma				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lung neoplasm malignant				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Malignant melanoma				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myelodysplastic syndrome				

subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myelofibrosis				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancreatic carcinoma				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Transitional cell carcinoma				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tumour haemorrhage				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tumour pain				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Aortic aneurysm				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Aortic aneurysm rupture				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Circulatory collapse				

subjects affected / exposed	1 / 32 (3.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Embolism				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypertension				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Jugular vein thrombosis				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lymphoedema				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Subclavian vein thrombosis				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Asthenia				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Death				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Disease progression				

subjects affected / exposed	1 / 32 (3.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Fatigue				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General physical health deterioration				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Malaise				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Mucosal inflammation				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Multiple organ dysfunction syndrome				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Systemic inflammatory response syndrome				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Immune system disorders				
Hypersensitivity				

subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Type IV hypersensitivity reaction				
subjects affected / exposed	1 / 32 (3.13%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Social circumstances				
Loss of personal independence in daily activities				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Acute pulmonary oedema				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchiectasis				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chronic obstructive pulmonary disease				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemoptysis				

subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pleural effusion				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia aspiration				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonitis				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Productive cough				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary oedema				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary thrombosis				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory distress				

subjects affected / exposed	0 / 32 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory failure			
subjects affected / exposed	0 / 32 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Abnormal behaviour			
subjects affected / exposed	0 / 32 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Confusional state			
subjects affected / exposed	0 / 32 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Depression			
subjects affected / exposed	0 / 32 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
Cytomegalovirus test positive			
subjects affected / exposed	0 / 32 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neutrophil count decreased			
subjects affected / exposed	0 / 32 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Oxygen saturation decreased			
subjects affected / exposed	0 / 32 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural			

complications				
Fall				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Femur fracture				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hip fracture				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Jaw fracture				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Multiple fractures				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Multiple injuries				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Acute coronary syndrome				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atrial fibrillation				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Cardiac arrest				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure chronic				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure congestive				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardio-respiratory arrest				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiopulmonary failure				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Coronary artery disease				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Left ventricular dysfunction				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sinus tachycardia				

subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Supraventricular tachycardia				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tachycardia				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ventricular tachycardia				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Cerebral haemorrhage				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebrovascular accident				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Generalised tonic-clonic seizure				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lethargy				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Paraparesis				

subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Status epilepticus				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Syncope				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Transient ischaemic attack				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular encephalopathy				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Anaemia				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Aplastic anaemia				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Autoimmune haemolytic anaemia				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Febrile neutropenia				

subjects affected / exposed	2 / 32 (6.25%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Haemolytic anaemia				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemorrhagic anaemia				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Leukopenia				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neutropenia				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancytopenia				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Thrombocytopenia				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Thrombocytopenic purpura				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Eye disorders				
Optic atrophy				

subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Retinal artery occlusion				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Retinal haemorrhage				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Abdominal pain				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Colitis				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Duodenal perforation				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Faecalith				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal haemorrhage				

subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Small intestinal obstruction				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Stomatitis				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Drug-induced liver injury				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatorenal syndrome				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hyperbilirubinaemia				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Portal vein thrombosis				

subjects affected / exposed	0 / 32 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	0 / 32 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Paraneoplastic pemphigus			
subjects affected / exposed	0 / 32 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Stevens-Johnson syndrome			
subjects affected / exposed	0 / 32 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Toxic epidermal necrolysis			
subjects affected / exposed	0 / 32 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urticaria			
subjects affected / exposed	0 / 32 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 32 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nephrolithiasis			
subjects affected / exposed	0 / 32 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal failure			

subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary tract inflammation				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Arthralgia				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pathological fracture				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Abdominal sepsis				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acinetobacter bacteraemia				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atypical pneumonia				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchiolitis				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Bronchopulmonary aspergillosis			
subjects affected / exposed	0 / 32 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Candida infection			
subjects affected / exposed	0 / 32 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cellulitis			
subjects affected / exposed	0 / 32 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Clostridium difficile infection			
subjects affected / exposed	0 / 32 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cytomegalovirus chorioretinitis			
subjects affected / exposed	0 / 32 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cytomegalovirus infection			
subjects affected / exposed	0 / 32 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Device related sepsis			
subjects affected / exposed	0 / 32 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dysentery			
subjects affected / exposed	0 / 32 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Escherichia urinary tract infection			

subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Febrile infection				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Herpes ophthalmic				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Herpes zoster				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Herpes zoster disseminated				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infective exacerbation of chronic obstructive airways disease				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Klebsiella sepsis				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lower respiratory tract infection				

subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lung infection				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Meningitis				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neutropenic infection				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oesophageal candidiasis				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peritonitis				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pharyngitis				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumocystis jirovecii infection				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumocystis jirovecii pneumonia				

subjects affected / exposed	1 / 32 (3.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	1 / 32 (3.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia cytomegaloviral				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Postoperative abscess				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Progressive multifocal leukoencephalopathy				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary sepsis				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory tract infection				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Septic shock				

subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sinusitis				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin infection				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Spinal cord infection				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Staphylococcal sepsis				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Staphylococcal skin infection				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Subcutaneous abscess				
subjects affected / exposed	1 / 32 (3.13%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Tuberculosis				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Upper respiratory tract infection				

subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urosepsis				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Varicella				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Decreased appetite				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dehydration				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diabetes mellitus				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Failure to thrive				
subjects affected / exposed	0 / 32 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypokalaemia				

subjects affected / exposed	0 / 32 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Total	OFA + BENDA	BENDA
Total subjects affected by non-serious adverse events			
subjects affected / exposed	320 / 342 (93.57%)	158 / 172 (91.86%)	162 / 170 (95.29%)
Vascular disorders			
Hypertension			
subjects affected / exposed	21 / 342 (6.14%)	10 / 172 (5.81%)	6 / 170 (3.53%)
occurrences (all)	0	10	6
Hypotension			
subjects affected / exposed	16 / 342 (4.68%)	9 / 172 (5.23%)	6 / 170 (3.53%)
occurrences (all)	0	9	7
Phlebitis			
subjects affected / exposed	16 / 342 (4.68%)	6 / 172 (3.49%)	10 / 170 (5.88%)
occurrences (all)	0	6	12
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	44 / 342 (12.87%)	17 / 172 (9.88%)	27 / 170 (15.88%)
occurrences (all)	0	26	31
Chills			
subjects affected / exposed	25 / 342 (7.31%)	9 / 172 (5.23%)	15 / 170 (8.82%)
occurrences (all)	0	12	19
Fatigue			
subjects affected / exposed	101 / 342 (29.53%)	41 / 172 (23.84%)	59 / 170 (34.71%)
occurrences (all)	0	53	69
Influenza like illness			
subjects affected / exposed	13 / 342 (3.80%)	9 / 172 (5.23%)	4 / 170 (2.35%)
occurrences (all)	0	9	6
Malaise			
subjects affected / exposed	15 / 342 (4.39%)	3 / 172 (1.74%)	12 / 170 (7.06%)
occurrences (all)	0	3	16
Mucosal inflammation			

subjects affected / exposed	24 / 342 (7.02%)	9 / 172 (5.23%)	14 / 170 (8.24%)
occurrences (all)	0	10	16
Oedema peripheral			
subjects affected / exposed	23 / 342 (6.73%)	9 / 172 (5.23%)	14 / 170 (8.24%)
occurrences (all)	0	15	15
Pyrexia			
subjects affected / exposed	78 / 342 (22.81%)	33 / 172 (19.19%)	44 / 170 (25.88%)
occurrences (all)	0	54	62
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	68 / 342 (19.88%)	38 / 172 (22.09%)	27 / 170 (15.88%)
occurrences (all)	0	42	31
Dyspnoea			
subjects affected / exposed	38 / 342 (11.11%)	14 / 172 (8.14%)	21 / 170 (12.35%)
occurrences (all)	0	16	23
Oropharyngeal pain			
subjects affected / exposed	14 / 342 (4.09%)	10 / 172 (5.81%)	3 / 170 (1.76%)
occurrences (all)	0	11	3
Psychiatric disorders			
Insomnia			
subjects affected / exposed	26 / 342 (7.60%)	15 / 172 (8.72%)	8 / 170 (4.71%)
occurrences (all)	0	18	8
Investigations			
Neutrophil count decreased			
subjects affected / exposed	26 / 342 (7.60%)	13 / 172 (7.56%)	13 / 170 (7.65%)
occurrences (all)	0	27	24
Platelet count decreased			
subjects affected / exposed	26 / 342 (7.60%)	12 / 172 (6.98%)	14 / 170 (8.24%)
occurrences (all)	0	15	18
Weight decreased			
subjects affected / exposed	31 / 342 (9.06%)	11 / 172 (6.40%)	20 / 170 (11.76%)
occurrences (all)	0	11	20
White blood cell count decreased			
subjects affected / exposed	20 / 342 (5.85%)	11 / 172 (6.40%)	9 / 170 (5.29%)
occurrences (all)	0	17	15
Injury, poisoning and procedural complications			

Infusion related reaction			
subjects affected / exposed	25 / 342 (7.31%)	19 / 172 (11.05%)	2 / 170 (1.18%)
occurrences (all)	0	27	2
Nervous system disorders			
Dizziness			
subjects affected / exposed	22 / 342 (6.43%)	14 / 172 (8.14%)	7 / 170 (4.12%)
occurrences (all)	0	16	7
Dysgeusia			
subjects affected / exposed	29 / 342 (8.48%)	9 / 172 (5.23%)	20 / 170 (11.76%)
occurrences (all)	0	9	20
Headache			
subjects affected / exposed	56 / 342 (16.37%)	31 / 172 (18.02%)	21 / 170 (12.35%)
occurrences (all)	0	40	27
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	77 / 342 (22.51%)	31 / 172 (18.02%)	46 / 170 (27.06%)
occurrences (all)	0	41	65
Leukopenia			
subjects affected / exposed	46 / 342 (13.45%)	25 / 172 (14.53%)	21 / 170 (12.35%)
occurrences (all)	0	43	31
Lymphopenia			
subjects affected / exposed	34 / 342 (9.94%)	17 / 172 (9.88%)	17 / 170 (10.00%)
occurrences (all)	0	25	18
Neutropenia			
subjects affected / exposed	141 / 342 (41.23%)	66 / 172 (38.37%)	74 / 170 (43.53%)
occurrences (all)	0	132	145
Thrombocytopenia			
subjects affected / exposed	77 / 342 (22.51%)	30 / 172 (17.44%)	46 / 170 (27.06%)
occurrences (all)	0	37	74
Eye disorders			
Vitreous floaters			
subjects affected / exposed	3 / 342 (0.88%)	1 / 172 (0.58%)	0 / 170 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	20 / 342 (5.85%)	9 / 172 (5.23%)	11 / 170 (6.47%)
occurrences (all)	0	10	12

Constipation			
subjects affected / exposed	72 / 342 (21.05%)	29 / 172 (16.86%)	40 / 170 (23.53%)
occurrences (all)	0	39	46
Diarrhoea			
subjects affected / exposed	75 / 342 (21.93%)	35 / 172 (20.35%)	40 / 170 (23.53%)
occurrences (all)	0	56	53
Dry mouth			
subjects affected / exposed	16 / 342 (4.68%)	7 / 172 (4.07%)	9 / 170 (5.29%)
occurrences (all)	0	9	10
Dyspepsia			
subjects affected / exposed	16 / 342 (4.68%)	9 / 172 (5.23%)	7 / 170 (4.12%)
occurrences (all)	0	10	7
Nausea			
subjects affected / exposed	155 / 342 (45.32%)	62 / 172 (36.05%)	93 / 170 (54.71%)
occurrences (all)	0	101	151
Stomatitis			
subjects affected / exposed	19 / 342 (5.56%)	6 / 172 (3.49%)	12 / 170 (7.06%)
occurrences (all)	0	7	13
Vomiting			
subjects affected / exposed	66 / 342 (19.30%)	25 / 172 (14.53%)	40 / 170 (23.53%)
occurrences (all)	0	36	58
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	10 / 342 (2.92%)	4 / 172 (2.33%)	4 / 170 (2.35%)
occurrences (all)	0	4	4
Erythema			
subjects affected / exposed	12 / 342 (3.51%)	7 / 172 (4.07%)	4 / 170 (2.35%)
occurrences (all)	0	11	4
Pruritus			
subjects affected / exposed	40 / 342 (11.70%)	24 / 172 (13.95%)	12 / 170 (7.06%)
occurrences (all)	0	32	19
Rash			
subjects affected / exposed	50 / 342 (14.62%)	33 / 172 (19.19%)	15 / 170 (8.82%)
occurrences (all)	0	47	16
Urticaria			

subjects affected / exposed	18 / 342 (5.26%)	13 / 172 (7.56%)	1 / 170 (0.59%)
occurrences (all)	0	14	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	25 / 342 (7.31%)	13 / 172 (7.56%)	12 / 170 (7.06%)
occurrences (all)	0	14	13
Back pain			
subjects affected / exposed	20 / 342 (5.85%)	13 / 172 (7.56%)	5 / 170 (2.94%)
occurrences (all)	0	13	5
Musculoskeletal pain			
subjects affected / exposed	7 / 342 (2.05%)	0 / 172 (0.00%)	5 / 170 (2.94%)
occurrences (all)	0	0	5
Myalgia			
subjects affected / exposed	15 / 342 (4.39%)	4 / 172 (2.33%)	9 / 170 (5.29%)
occurrences (all)	0	4	10
Pain in extremity			
subjects affected / exposed	19 / 342 (5.56%)	11 / 172 (6.40%)	8 / 170 (4.71%)
occurrences (all)	0	14	10
Infections and infestations			
Bronchitis			
subjects affected / exposed	30 / 342 (8.77%)	19 / 172 (11.05%)	11 / 170 (6.47%)
occurrences (all)	0	23	13
Herpes zoster			
subjects affected / exposed	20 / 342 (5.85%)	9 / 172 (5.23%)	10 / 170 (5.88%)
occurrences (all)	0	9	11
Nasopharyngitis			
subjects affected / exposed	42 / 342 (12.28%)	27 / 172 (15.70%)	14 / 170 (8.24%)
occurrences (all)	0	36	17
Oral herpes			
subjects affected / exposed	19 / 342 (5.56%)	9 / 172 (5.23%)	10 / 170 (5.88%)
occurrences (all)	0	9	10
Sinusitis			
subjects affected / exposed	17 / 342 (4.97%)	10 / 172 (5.81%)	7 / 170 (4.12%)
occurrences (all)	0	11	7
Upper respiratory tract infection			

subjects affected / exposed	29 / 342 (8.48%)	12 / 172 (6.98%)	15 / 170 (8.82%)
occurrences (all)	0	17	16
Urinary tract infection			
subjects affected / exposed	21 / 342 (6.14%)	11 / 172 (6.40%)	7 / 170 (4.12%)
occurrences (all)	0	11	9
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	69 / 342 (20.18%)	24 / 172 (13.95%)	44 / 170 (25.88%)
occurrences (all)	0	28	53
Diabetes mellitus			
subjects affected / exposed	3 / 342 (0.88%)	1 / 172 (0.58%)	0 / 170 (0.00%)
occurrences (all)	0	1	0
Hyperglycaemia			
subjects affected / exposed	17 / 342 (4.97%)	9 / 172 (5.23%)	8 / 170 (4.71%)
occurrences (all)	0	11	9
Hyperkalaemia			
subjects affected / exposed	3 / 342 (0.88%)	0 / 172 (0.00%)	1 / 170 (0.59%)
occurrences (all)	0	0	1
Hypokalaemia			
subjects affected / exposed	27 / 342 (7.89%)	11 / 172 (6.40%)	15 / 170 (8.82%)
occurrences (all)	0	14	20

Non-serious adverse events	Optional OFA		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 32 (65.63%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	5 / 32 (15.63%)		
occurrences (all)	6		
Hypotension			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Phlebitis			
subjects affected / exposed	0 / 32 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			

Asthenia subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0		
Chills subjects affected / exposed occurrences (all)	1 / 32 (3.13%) 1		
Fatigue subjects affected / exposed occurrences (all)	5 / 32 (15.63%) 5		
Influenza like illness subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0		
Malaise subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0		
Mucosal inflammation subjects affected / exposed occurrences (all)	1 / 32 (3.13%) 2		
Oedema peripheral subjects affected / exposed occurrences (all)	0 / 32 (0.00%) 0		
Pyrexia subjects affected / exposed occurrences (all)	2 / 32 (6.25%) 2		
Respiratory, thoracic and mediastinal disorders			
Cough subjects affected / exposed occurrences (all)	6 / 32 (18.75%) 8		
Dyspnoea subjects affected / exposed occurrences (all)	4 / 32 (12.50%) 5		
Oropharyngeal pain subjects affected / exposed occurrences (all)	1 / 32 (3.13%) 1		
Psychiatric disorders			

Insomnia subjects affected / exposed occurrences (all)	3 / 32 (9.38%) 3		
Investigations Neutrophil count decreased subjects affected / exposed occurrences (all) Platelet count decreased subjects affected / exposed occurrences (all) Weight decreased subjects affected / exposed occurrences (all) White blood cell count decreased subjects affected / exposed occurrences (all)	 0 / 32 (0.00%) 0 0 / 32 (0.00%) 0 0 / 32 (0.00%) 0 0 / 32 (0.00%) 0		
Injury, poisoning and procedural complications Infusion related reaction subjects affected / exposed occurrences (all)	 4 / 32 (12.50%) 4		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all) Dysgeusia subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all)	 1 / 32 (3.13%) 1 0 / 32 (0.00%) 0 4 / 32 (12.50%) 5		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) Leukopenia	 0 / 32 (0.00%) 0 		

subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Lymphopenia			
subjects affected / exposed	0 / 32 (0.00%)		
occurrences (all)	0		
Neutropenia			
subjects affected / exposed	3 / 32 (9.38%)		
occurrences (all)	4		
Thrombocytopenia			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Eye disorders			
Vitreous floaters			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	2		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Constipation			
subjects affected / exposed	4 / 32 (12.50%)		
occurrences (all)	4		
Diarrhoea			
subjects affected / exposed	3 / 32 (9.38%)		
occurrences (all)	3		
Dry mouth			
subjects affected / exposed	0 / 32 (0.00%)		
occurrences (all)	0		
Dyspepsia			
subjects affected / exposed	0 / 32 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	5 / 32 (15.63%)		
occurrences (all)	6		
Stomatitis			

subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	3		
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	2		
Erythema			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	2		
Pruritus			
subjects affected / exposed	4 / 32 (12.50%)		
occurrences (all)	4		
Rash			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	2		
Urticaria			
subjects affected / exposed	4 / 32 (12.50%)		
occurrences (all)	4		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 32 (0.00%)		
occurrences (all)	0		
Back pain			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	2		
Musculoskeletal pain			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	2		
Myalgia			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	2		
Pain in extremity			

subjects affected / exposed	0 / 32 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 32 (0.00%)		
occurrences (all)	0		
Herpes zoster			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Nasopharyngitis			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Oral herpes			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		
Sinusitis			
subjects affected / exposed	0 / 32 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	5 / 32 (15.63%)		
occurrences (all)	5		
Urinary tract infection			
subjects affected / exposed	3 / 32 (9.38%)		
occurrences (all)	4		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	3		
Diabetes mellitus			
subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	2		
Hyperglycaemia			
subjects affected / exposed	0 / 32 (0.00%)		
occurrences (all)	0		
Hyperkalaemia			

subjects affected / exposed	2 / 32 (6.25%)		
occurrences (all)	3		
Hypokalaemia			
subjects affected / exposed	1 / 32 (3.13%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 November 2009	Logo updated to describe meaning of COMPLEMENT. Sponsor information page: Medical Monitor contact information updated. Addition of secondary endpoint: Overall response rate to optional ofatumumab monotherapy in subjects in Arm B who progress during or following single-agent bendamustine. Spelling correction in the Exclusion Criteria: fludaranine replaced by fludarabine and addition of criteria excluding prior treatment with anti-CD20 mAb within 3 months of randomization. Administered bendamustine therapy as monotherapy or in combination with ofatumumab for up to 8 cycles. There were a total of 12 ofatumumab infusions in Arm A. Ofatumumab was given on day 1 of each cycle of bendamustine as long as subjects in Arm A received bendamustine. Once subjects in Arm A completed bendamustine therapy, the remaining doses of ofatumumab were be given monthly until all 12 doses were completed.
12 May 2010	Introduction includes additional rationale for infusion of 1000 mg dose upon first infusion in and 2000 mg dose upon 2nd infusion (for those who receive ofatumumab following PD in Arm B) at protocol defined rate. Inclusion criterion #1 updated: Removed reference to bulky stage. Clarified screening procedures. Inclusion criterion #2 updated: to allow CT imaging performed at least 60 days after the last dose of rituximab-based therapy. Modified text for prior rituximab infusions. Exclusion criterion #3 updated timeframe from previous autologous stem cell transplant, or fludarabine therapy, or radioimmunotherapy from past 12 months to last 6 months. Exclusion criterion #5 updated timeframe for high dose steroids (7 consecutive days) and dose of prednisone before randomization (100 mg). Exclusion criterion #7 update to exclude prior use of any monoclonal antibody (other than anti- CD20) within 3 months of randomization and anti-CD20 therapy first dose was administered 60 days prior to randomization. Exclusion criteria #15 updated: specifies liver metastases related to indolent NHL. Exclusion criterion #18 updated to include hypersensitivity to bendamustine and mannitol. Removed exclusion criterion #20 since it duplicated criterion #7. Subjects in Arm B who chose to receive optional ofatumumab monotherapy received ofatumumab 1000 mg for the first dose. CT scans, lymphoma symptoms, and response assessments will be done Days 84, 168, and 252 (±7 days). Whole body CT scan (contrast imaging of neck when lesion is palpable, thorax, abdomen, pelvis). Rmoved mention of physical examination as part of CR assessment. Updated FACT-Lym Version 4, removed FACT-G Patient Reported Outcomes (PRO) questionnaire. HACA test done before first dose of ofatumumab.

19 January 2012	CT scans may be whole body or done according to local practice. No required bone marrow aspirate Known and exploratory prognostic markers and exploratory pharmacogenetic research objectives clarified. Inclusion Criterion #1: Type of previous biopsy changed from "lymph node" to "tissue" biopsy. Inclusion Criterion #1 clarified. Tumor verified to be CD20+ positive from a previous or current tissue biopsy. No longer excluded fludarabine and radioimmunotherapy. No longer excluded external beam radiation therapy to pelvis and to bony disease to the cranium, mediastinum, and axilla, or > 3 vertebral bodies. Removed Exclusion criterion restricting anti-CD20 antibody within the last 60 days. Copy of documentation confirming PD (for example, an imaging report, clinical documentation) after subject deemed unresponsive or relapsed to rituximab-based regimen was required. Follow-up visits begin 2 months after PD is confirmed by CT scan. For all other responses, follow-up visits begin on Day 336 (this is 3 months after Day 252) for both arms. Withdrawal Criteria: If a subject withdrew from study drug but did not withdraw from the study, the subject was expected to complete all scheduled visits without study drug. The subject may then enter follow-up.
07 February 2013	Edited text due to updates found in Investigator Brochure update. Correction in footnotes to Time and Events Table (Appendix 1): baseline CT scans required ≤1 month of randomization. Correct reference for Table updated. High dose steroids ≥ 25 mg prednisolone/day (or equivalent) for 7 consecutive days were excluded. Updated from excluding ≥ 100 mg prednisolone/day (or equivalent). All SAEs regardless of causality were reported from 61 days after the last dose of investigational product to the end of the follow-up period or until initiation of subsequent antilymphoma therapy is initiated. Any SAE brought to the investigator's attention after the start of subsequent anti-lymphoma therapy and considered by the investigator as possibly related to either ofatumumab or bendamustine were to be reported to GSK. Additional biochemistry testing added to time and events table for ofatumumab monotherapy following progression in Arm B. For Japan only: additional directions for Hepatitis monitoring added to an Appendix. Investigator Brochure reference updated.
07 February 2013	At the request of the French regulatory agency, safety related information from the Study Procedures Manual (SPM) was added.
02 December 2013	Added additional instructions for monitoring subjects who were HBsAg negative, anti-HBc positive and HBV DNA negative. This instruction was added to the relevant Time and Events tables. Exclusion criteria now specified that physician experienced in care and management of subjects with Hepatitis B manage/treat subjects who were anti-HBc positive must be consulted. Changes for countries using Amendment 4 included specific details on how to manage AEs and SAEs such as infusion reactions, tumor lysis syndrome, progressive multifocal leukoencephalopathy and hepatitis were described.
07 July 2015	Authors and Sponsor Contact Information Updated Table of Contents updated to include Appendix 15: Protocol Changes for Amendment #7 from Amendment #6. Total number of events increased to 259 events. Total study duration increased to 77 months. Total accrual rate decreased to 5.1pt/month. Clarification of randomization strategy. An Interim Analysis added for efficacy when two thirds of IRR events occurred. Details of a further Independent Data Monitoring Committee (IDMC) added to review the safety, efficacy, and futility data and recommended whether the study should continue without any changes, be stopped to further enrollment, or be terminated. Liver stopping criteria updated to reflect stopping criteria applies to all patients on study, regardless of Arm assignment. Clarification of instructions regarding how patients moved into Survival Follow-Up. Amendment Republished due to typographical error.

18 March 2016	The purpose of this protocol amendment was to: - Delete or replace references to GSK or its staff with that of Novartis and its authorized agents to align with the change of sponsorship - Make administrative changes to align with Novartis processes and procedures
13 April 2017	The purpose of amendment 9 was to revise the total number of events required for the primary analysis of the primary end point PFS. The primary analysis was planned after reaching 259 PFS events as determined by an Independent Review Committee (IRC). Based on the current status of the study and PFS event count by IRC, it was highly unlikely that the 259 PFS events wiould be achieved.

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.

Due to EudraCT system limitations, which EMA is aware of, data using 999 as data points in this record are not an accurate representation of the clinical trial results. Please use https://www.novctrd.com/CtrdWeb/home.nov for complete trial results.

Notes: