Clinical trial results:
A PHASE 3B RANDOMIZED STUDY OF LENALIDOMIDE (CC-5013) PLUS RITUXIMAB MAINTENANCE THERAPY FOLLOWED BY LENALIDOMIDE SINGLEAGENT MAINTENANCE VERSUS RITUXIMAB MAINTENANCE IN SUBJECTS WITH RELAPSED/REFRACTORY FOLLICULAR, MARGINAL ZONE OR MANTLE CELL LYMPHOMA

Summary

EudraCT number	2017-002290-19
Trial protocol	DE
Global end of trial date	17 September 2024

Results information

Result version number	v1 (current)
This version publication date	23 October 2025
First version publication date	23 October 2025

Trial information

Trial identification

Sponsor protocol code	cc-5013-nhl-008

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Bristol-Myers Squibb
Sponsor organisation address	Chaussee de la Hulpe 185, Brussels, Belgium, 1170
Public contact	Global Submission Management - Clinical Trials, Bristol-Myers Squibb International Corporation, mg-gsm-ct@bms.com
Scientific contact	Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, mg-gsm-ct@bms.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	
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	30 September 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 September 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to compare the efficacy of lenalidomide plus rituximab combination maintenance therapy (for 18 cycles) followed by optional lenalidomide single-agent maintenance (to progression) versus rituximab single-agent maintenance (for 18 cycles) after 12 cycles of induction therapy with lenalidomide plus rituximab, in subjects with relapsed/refractory FL grades 1-3b, transformed FL, MZL or MCL. Efficacy determinations will be based upon PFS as the primary endpoint, using a modification of the IWG 1999 criteria.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial participants were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 April 2014
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	United States: 459
Country: Number of subjects enrolled	Germany: 44
Worldwide total number of subjects	503
EEA total number of subjects	44

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)	209

From 65 to 84 years	240
85 years and over	54

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

503 patients enrolled and 267 patients were randomized to maintenance and 266 patients were treated.

All participants started in the induction period; only those who did not progress after 12 cycles of treatment were randomized to receive treatment in the maintenance period.

Period 1

Period 1 title	Induction Period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Arm title	Induction Period: Lenalidomide - Rituximab

Arm description:

Induction Period (12 cycles): participants received lenalidomide 20 mg (10 mg if creatinine clearance ≥ 30 mL/min but < 60 mL/min) once daily on Days 1 to 21 of every 28-day Cycle for Cycles 1 to 12 AND rituximab 375 mg/m2 every week in Cycle 1 (Days 1, 8, 15, and 22) and Day 1 of every 28-day Cycle for Cycles 3, 5, 7, 9, and 11

Arm type	Experimental
Investigational medicinal product name	Rituximab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Rituximab 375 mg/m2 every week in Cycle 1 (Days 1, 8, 15, and 22) and Day 1 of every 28-day Cycle for Cycles 3, 5, 7, 9, and 11

Investigational medicinal product name	Lenalidomide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Lenalidomide 20 mg 10 mg if creatinine clearance ≥ 30 mL/min but < 60 mL/min) once daily on Days 1 to 21 of every 28-day Cycle for Cycles 1 to 12

Number of subjects in period 1	Induction Period: Lenalidomide - Rituximab
Started	503
Treated	500
Completed	284
Not completed	219

Adverse event, serious fatal	111
Consent withdrawn by subject	60
Other Reasons	13
Adverse event, non-fatal	20
Progressive Disease	4
Lost to follow-up	10
Protocol deviation	1

Period 2

Period 2 title	Maintenance Period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A: Lenalidomide + Rituximab

Arm description:

Maintenance Period (18 Cycles): lenalidomide 10 mg once daily on Days 1 to 21 of every 28-day Cycle for Cycles 13 to 30 AND rituximab 375 mg/m2 on Day 1 of every 28-day Cycle for Cycles 13, 15, 17, 19, 21, 23, 25, 27, and 29. Followed by Optional Maintenance Period (up to PD): Lenalidomide 10 mg once daily on Days 1 to 21 of every 28-day Cycle up to PD. This treatment will be at the discretion of the participant and the investigator.

Arm type	Experimental
Investigational medicinal product name	Rituximab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Rituximab 375 mg/m2 on Day 1 of every 28-day Cycle for Cycles 13, 15, 17, 19, 21, 23, 25, 27, and 29.

Investigational medicinal product name	Lenalidomide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

18 Cycles: lenalidomide 10 mg once daily on Days 1 to 21 of every 28-day Cycle for Cycles 13 to 30. Followed by Optional Maintenance Period (up to PD): Lenalidomide 10 mg once daily on Days 1 to 21 of every 28-day Cycle up to PD.

Arm title	Arm B: Rituximab

Arm description:

Maintenance Period (18 Cycles): participants received rituximab 375 mg/m2 on Day 1 of every 28-day Cycle for Cycles 13, 15, 17, 19, 21, 23, 25, 27, and 29

Arm type	Experimental

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

Dosage and administration details:

18 Cycles: rituximab 375 mg/m2 on Day 1 of every 28-day Cycle for Cycles 13, 15, 17, 19, 21, 23, 25, 27, and 29

Number of subjects in period 2[1]	Arm A: Lenalidomide + Rituximab	Arm B: Rituximab
Started	135	132
Treated	134	132
Completed	78	89
Not completed	57	43
Adverse event, serious fatal	15	3
Consent withdrawn by subject	18	4
Other Reasons	8	5
Adverse event, non-fatal	7	7
Progressive Disease	6	23
Lost to follow-up	2	-
Protocol deviation	1	1

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: All participants received treatment in the Induction Period and then were moved into the Maintenance Period and received treatment in one of two arms. This accounts for the change in the number of participants per arm in this period compared to the previous period.

Baseline characteristics

Reporting groups	
Reporting group title	Induction Period

Reporting group description: -

Reporting group values	Induction Period	Total	
Number of subjects	503	503	
Age Categorical Units: Participants			
<=18 years	0	0	
Between 18 and 65 years	209	209	
>=65 years	294	294	
Age continuous Units: years			
geometric mean	66.5		
standard deviation	± 10.43	-	
Sex: Female, Male Units: Participants			
Female	215	215	
Male	288	288	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	1	1	
Asian	4	4	
Native Hawaiian or Other Pacific Islander	1	1	
Black or African American	17	17	
White	468	468	
More than one race	0	0	
Unknown or Not Reported	12	12	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	33	33	
Not Hispanic or Latino	463	463	
Unknown or Not Reported	7	7	

End points

End points reporting groups

Reporting group title	Induction Period: Lenalidomide - Rituximab
Reporting group description:	
Induction Period (12 cycles): participants received lenalidomide 20 mg (10 mg if creatinine clearance ≥ 30 mL/min but < 60 mL/min) once daily on Days 1 to 21 of every 28-day Cycle for Cycles 1 to 12 AND rituximab 375 mg/m2 every week in Cycle 1 (Days 1, 8, 15, and 22) and Day 1 of every 28-day Cycle for Cycles 3, 5, 7, 9, and 11	
Reporting group title	Arm A: Lenalidomide + Rituximab
Reporting group description:	
Maintenance Period (18 Cycles): lenalidomide 10 mg once daily on Days 1 to 21 of every 28-day Cycle for Cycles 13 to 30 AND rituximab 375 mg/m2 on Day 1 of every 28-day Cycle for Cycles 13, 15, 17, 19, 21, 23, 25, 27, and 29. Followed by Optional Maintenance Period (up to PD): Lenalidomide 10 mg once daily on Days 1 to 21 of every 28-day Cycle up to PD. This treatment will be at the discretion of the participant and the investigator.	
Reporting group title	Arm B: Rituximab
Reporting group description:	
Maintenance Period (18 Cycles): participants received rituximab 375 mg/m2 on Day 1 of every 28-day Cycle for Cycles 13, 15, 17, 19, 21, 23, 25, 27, and 29	

Primary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)
End point description:	
Progression free survival (PFS) is defined as the time from the date of first dose of maintenance therapy to the date of the first objective documentation of tumor progression or death due to any cause. Analysis was based on Kaplan Meier estimates. The PFS events were determined using a modification of the IWG 1999 criteria.	
End point type	Primary
End point timeframe:	
From the first dose date of maintenance therapy to objective disease progression or death from any cause, whichever occurs first (up to approximately 432 weeks)	

End point values	Arm A: Lenalidomide + Rituximab	Arm B: Rituximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	135	132		
Units: Weeks				
median (confidence interval 95%)	263.1 (166.1 to 99999)	229.1 (173.7 to 99999)		

Statistical analyses

Statistical analysis title	PFS
Comparison groups	Arm A: Lenalidomide + Rituximab v Arm B: Rituximab

Number of subjects included in analysis	267
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.3296
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	1.2

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

Overall Survival (OS) is defined as the time between the first dose date of maintenance therapy and death from any cause. Participants who complete the study and are still alive at the time of the clinical data cutoff date will be censored at the last visit date or the last contact date, whichever is later. Participants who were lost to follow-up prior to the clinical data cut-off date will also be censored at the time of the last contact. Analysis was based on Kaplan Meier estimates and Hazard Ratio (HR).

"99999"=N/A

End point type	Secondary

End point timeframe:

From the first dose date of maintenance therapy to death from any cause (up to approximately 480 weeks)

End point values	Arm A: Lenalidomide + Rituximab	Arm B: Rituximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	135	132		
Units: Weeks				
median (confidence interval 95%)	99999 (439.4 to 99999)	99999 (395.7 to 99999)		

Statistical analyses

Statistical analysis title	OS
Comparison groups	Arm A: Lenalidomide + Rituximab v Arm B: Rituximab

Number of subjects included in analysis	267
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.1222
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	1.1

Secondary: Improvement of Response (IOR)

End point title	Improvement of Response (IOR)

End point description:

Improvement of Response (IOR) is the percentage of participants with improved tumor response during the maintenance phase (converted from partial response at end of induction to complete response or complete response unconfirmed as best response) and participants who converted from stable disease at the end of induction period to partial response or better as best response during maintenance phase.

End point type	Secondary

End point timeframe:

From the first dose date of maintenance therapy to death from any cause (up to approximately 432 weeks)

End point values	Arm A: Lenalidomide + Rituximab	Arm B: Rituximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	135[1]	132[2]		
Units: Percentage of participants				
number (confidence interval 95%)	20 (13.6 to 27.7)	11.4 (6.5 to 18.0)		

Notes:

[1] - Number (%)
95% Confidence Interval

[2] - Number (%)
95% Confidence Interval

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Response Rate (ORR)

End point title	Overall Response Rate (ORR)

End point description:

The overall response rate (ORR) is defined as the percentage of participants with a best response of at least PR (including CR, CRu and PR) after the first dose date of maintenance therapy and prior to any treatment change.

End point type	Secondary

End point timeframe:

From the first dose date of maintenance therapy up to CR, CRu, PR, or treatment change (up to approximately 432 weeks)

End point values	Arm A: Lenalidomide + Rituximab	Arm B: Rituximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	135[3]	132[4]		
Units: Percentage of participants				
number (confidence interval 95%)	85.2 (78.1 to 90.7)	79.5 (71.7 to 86.1)		

Notes:

[3] - Number (%)
95% Confidence Interval
[4] - Number (%)
95% Confidence Interval

Statistical analyses

No statistical analyses for this end point

Secondary: Complete Response Rate (CRR)

End point title	Complete Response Rate (CRR)

End point description:

Best Complete Response Rate (CRR), defined as the proportion of participants with a best response of at least CRu (including CR and CRu) after the first dose date of maintenance therapy and prior to any treatment change.

End point type	Secondary

End point timeframe:

From the first dose date of maintenance therapy up to CR or CRu (up to approximately 432 weeks)

End point values	Arm A: Lenalidomide + Rituximab	Arm B: Rituximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	135[5]	132[6]		
Units: Percentage of participants				
number (confidence interval 95%)	60.7 (52.0 to 69.0)	58.39 (49.4 to 66.8)		

Notes:

[5] - Number (%)
95% Confidence Interval
[6] - Number (%)
95% Confidence Interval

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR)

End point title	Duration of Response (DOR)

End point description:

DOR is from initial response (at least CRu) after the first dose date of maintenance therapy and prior to treatment change to documented disease progression or death. Participants who have not progressed or died at the time of the clinical data cutoff date will be censored at the last assessment showing no progression. Participants who change treatment without evidence of disease progression will be censored at the last assessment showing no progression prior to treatment change. Analysis was based on Kaplan Meier estimates.

"99999"=N/A

End point type	Secondary

End point timeframe:

From the initial response (at least PR) after the first dose date of maintenance therapy and prior to treatment change to documented disease progression or death, whichever occurs first (up to approximately 432 weeks)

End point values	Arm A: Lenalidomide + Rituximab	Arm B: Rituximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	135	132		
Units: Weeks				
median (confidence interval 95%)	60.7 (52.0 to 69.0)	58.39 (49.4 to 66.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Next Anti-lymphoma Treatment

End point title	Time to Next Anti-lymphoma Treatment

End point description:

Time to next anti-lymphoma treatment is defined as the time from the first dose date of maintenance therapy to the time of first documented administration of new anti-lymphoma therapy. Participants without new treatment therapy will be censored at the last visit. Analysis was based on Kaplan Meier estimates.

"99999"=N/A

End point type	Secondary

End point timeframe:

From the first dose date of maintenance therapy to the time of first documented administration of new anti-lymphoma therapy (up to approximately 300 weeks)

End point values	Arm A: Lenalidomide + Rituximab	Arm B: Rituximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	135	132		
Units: Weeks				
median (confidence interval 95%)	99999 (300.4 to 99999)	99999 (283.4 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Histological Transformation

End point title	Time to Histological Transformation

End point description:

Time to histological transformation is defined as from the first dose date of maintenance therapy to the time of histological transformation as measured based on documentation of histological transformation (as assessed by the investigator). Analysis was based on Kaplan Meier estimates.

In case of clinical suspicion of transformation, including rapid disease progression, unexpected changes in "B" symptoms or rapidly increasing LDH, a biopsy should be performed. In this clinical trial, histological transformation will be considered disease progression. This endpoint will not be calculated for participants randomized with transformed Follicular Lymphoma (tFL).

"99999"=N/A

End point type	Secondary

End point timeframe:

From the first dose date of maintenance therapy to the time of histological transformation (up to approximately 432 weeks)

End point values	Arm A: Lenalidomide + Rituximab	Arm B: Rituximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	133	129		
Units: Weeks				
median (confidence interval 95%)	99999 (99999 to 99999)	99999 (99999 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Complete Response (DOCR)

End point title	Duration of Complete Response (DOCR)

End point description:

Duration of complete response (DOCR) is calculated as the time from the initial response (CR or CRu) after the first dose date of maintenance therapy and prior to treatment change to documented disease

progression or death. Analysis was based on Kaplan Meier estimates. Participants who have not progressed or died at the time of the clinical data cutoff date will be censored at the last assessment showing no progression. Participants who change treatment without evidence of disease progression will be censored at the last assessment showing no progression prior to treatment change.

"99999"=N/A

End point type	Secondary

End point timeframe:

From the initial CR/CRu after the first dose date of maintenance therapy and prior to treatment change to documented disease progression or death, whichever occurs first (up to approximately 432 weeks)

End point values	Arm A: Lenalidomide + Rituximab	Arm B: Rituximab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	85	82		
Units: Weeks				
median (confidence interval 95%)	298.0 (176.0 to 99999)	99999 (221.1 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Participants Experiencing Treatment Emergent Adverse Events (TEAEs)

End point title	Participants Experiencing Treatment Emergent Adverse Events (TEAEs)

End point description:

Number of participants experiencing AEs, SAEs, AEs leading to study discontinuation, and AEs of interest (AEIs). An Adverse Event (AE) is defined as any new untoward medical occurrence or worsening of a preexisting medical condition in a clinical investigation participant administered study treatment and that does not necessarily have a causal relationship with this treatment. SAEs is any untoward medical occurrence that, at any dose: results in death; is life-threatening; requires inpatient hospitalization; results significant disability; or is a congenital anomaly/birth defect. TEAEs are defined as AEs with an onset date on or after the first dose of study treatment up to 30 days after the last dose of study treatment in the study, or if a pre-existing condition worsens in severity or becomes serious after receiving the first dose of study treatment.

End point type	Secondary

End point timeframe:

From first dose up to 30 days after last dose (up to approximately 64 weeks for induction period and 427 weeks for maintenance period)

End point values	Induction Period: Lenalidomide - Rituximab	Arm A: Lenalidomide + Rituximab	Arm B: Rituximab	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	500	134	132	
Units: Participants				
TEAE	499	133	120	

Serious TEAE	172	57	22	

Statistical analyses

No statistical analyses for this end point

Secondary: Participants Experiencing Adverse Events Related to Vital Signs

End point title	Participants Experiencing Adverse Events Related to Vital Signs

End point description:

The number of participants who experienced adverse events related to vital sign measurements.

End point type	Secondary

End point timeframe:

From first dose up to 30 days after last dose (up to approximately 64 weeks for induction period and 427 weeks for maintenance period)

End point values	Induction Period: Lenalidomide - Rituximab	Arm A: Lenalidomide + Rituximab	Arm B: Rituximab	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	500	134	132	
Units: Participants				
Hypertension	34	9	6	
Hypotension	22	4	5	
Hypoxia	5	2	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Participants with Grade 3 or Grade 4 Hematology Parameters

End point title	Participants with Grade 3 or Grade 4 Hematology Parameters

End point description:

Clinical laboratory values in induction period include any laboratory values that are taken after the first dose date of induction therapy through 28 days after the last dose date of induction therapy or before the first dose date of maintenance therapy, whichever is earlier. Graded according to the NCI CTCAE version 4.03, except for tumor flare reaction, which is accessed using NCI CTCAE version 3.0. Participants with zero maximum grade are excluded.

End point type	Secondary

End point timeframe:

From first dose up to 30 days after last dose (up to approximately 64 weeks for induction period and 427 weeks for maintenance period)

End point values	Induction Period: Lenalidomide - Rituximab	Arm A: Lenalidomide + Rituximab	Arm B: Rituximab	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	500	134	132	
Units: Participants				
Anemia - Grade 3	31	7	0	
Leukopenia - Grade 3	101	19	6	
Thrombocytopenia - Grade 3	29	2	1	
Neutropenia - Grade 3	103	24	10	
Lymphopenia - Grade 3	126	31	21	
Anemia - Grade 4	0	0	0	
Leukopenia - Grade 4	17	5	0	
Thrombocytopenia - Grade 4	7	0	0	
Neutropenia - Grade 4	94	25	6	
Lymphopenia - Grade 4	20	10	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Participants with Grade 3 or Grade 4 Serum Chemistry Parameters

End point title	Participants with Grade 3 or Grade 4 Serum Chemistry Parameters

End point description:

Clinical laboratory values in induction period include any laboratory values that are taken after the first dose date of induction therapy through 28 days after the last dose date of therapy. Graded according to the NCI CTCAE version 4.03, except for tumor flare reaction, which is accessed using NCI CTCAE version 3.0. Participants with zero maximum grade are excluded.

End point type	Secondary

End point timeframe:

From first dose up to 30 days after last dose (up to approximately 64 weeks for induction period and 427 weeks for maintenance period)

End point values	Induction Period: Lenalidomide - Rituximab	Arm A: Lenalidomide + Rituximab	Arm B: Rituximab	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	500	134	132	
Units: Participants				
Hypokalemia - Grade 3	30	8	4	
Hyperkalemia- Grade 3	4	0	1	
Hypocalcemia - Grade 3	7	1	0	
Hypercalcemia - Grade 3	7	0	0	

Hypophosphatemia - Grade 3	17	6	2	
Hypercreatininemia - Grade 3	3	1	0	
Hyperuricemia - Grade 3	40	13	20	
Alanine Aminotransferase Increased - Grade 3	14	3	0	
Aspartate Aminotransferase Increased - Grade 3	9	1	0	
Hyperbilirubinemia - Grade 3	5	3	1	
Hypokalemia - Grade 4	4	0	0	
Hyperkalemia- Grade 4	1	2	0	
Hypocalcemia - Grade 4	5	5	2	
Hypercalcemia - Grade 4	3	5	0	
Hypophosphatemia - Grade 4	1	1	1	
Hypercreatininemia - Grade 4	1	2	0	
Hyperuricemia - Grade 4	0	4	0	
Alanine Aminotransferase Increased - Grade 4	0	0	0	
Aspartate Aminotransferase Increased - Grade 4	0	0	0	
Hyperbilirubinemia - Grade 4	1	1	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All-cause mortality was assessed from first dose to study completion (up to approx. 10 years). SAEs & AEs were assessed from first dose to 30 days following last dose (up to approx. 64 weeks for induction period & 427 weeks for maintenance period).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups

Reporting group title	Induction Period: Lenalidomide - Rituximab

Reporting group description:

Induction Period (12 cycles): participants received lenalidomide 20 mg (10 mg if creatinine clearance ≥ 30 mL/min but < 60 mL/min) once daily on Days 1 to 21 of every 28-day Cycle for Cycles 1 to 12 AND rituximab 375 mg/m2 every week in Cycle 1 (Days 1, 8, 15, and 22) and Day 1 of every 28-day Cycle for Cycles 3, 5, 7, 9, and 11

Reporting group title	Maintenance Period: Arm A

Reporting group description:

Maintenance Period (18 Cycles): lenalidomide 10 mg once daily on Days 1 to 21 of every 28-day Cycle for Cycles 13 to 30 AND rituximab 375 mg/m2 on Day 1 of every 28-day Cycle for Cycles 13, 15, 17, 19, 21, 23, 25, 27, and 29. Followed by Optional Maintenance Period (up to PD): Lenalidomide 10 mg once daily on Days 1 to 21 of every 28-day Cycle up to PD. This treatment will be at the discretion of the participant and the investigator.

Reporting group title	Maintenance Period: Arm B

Reporting group description:

Maintenance Period (18 Cycles): participants received rituximab 375 mg/m2 on Day 1 of every 28-day Cycle for Cycles 13, 15, 17, 19, 21, 23, 25, 27, and 29

Serious adverse events	Induction Period: Lenalidomide - Rituximab	Maintenance Period: Arm A	Maintenance Period: Arm B
Total subjects affected by serious adverse events			
subjects affected / exposed	172 / 500 (34.40%)	57 / 134 (42.54%)	22 / 132 (16.67%)
number of deaths (all causes)	112	26	32
number of deaths resulting from adverse events	13	1	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma			
subjects affected / exposed	0 / 500 (0.00%)	1 / 134 (0.75%)	0 / 132 (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
Central nervous system lymphoma			

subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder transitional cell carcinoma			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	1 / 132 (0.76%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bowen's disease			
subjects affected / exposed	3 / 500 (0.60%)	3 / 134 (2.24%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer			
subjects affected / exposed	0 / 500 (0.00%)	1 / 134 (0.75%)	0 / 132 (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
Basal cell carcinoma			
subjects affected / exposed	8 / 500 (1.60%)	10 / 134 (7.46%)	5 / 132 (3.79%)
occurrences causally related to treatment / all	0 / 9	0 / 13	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lip squamous cell carcinoma			
subjects affected / exposed	0 / 500 (0.00%)	0 / 134 (0.00%)	1 / 132 (0.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large granular lymphocytosis			
subjects affected / exposed	1 / 500 (0.20%)	1 / 134 (0.75%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Invasive ductal breast carcinoma			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	1 / 132 (0.76%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diffuse large B-cell lymphoma recurrent			

subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphoma			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sebaceous carcinoma			
subjects affected / exposed	0 / 500 (0.00%)	0 / 134 (0.00%)	1 / 132 (0.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	1 / 500 (0.20%)	1 / 134 (0.75%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myelodysplastic syndrome			
subjects affected / exposed	1 / 500 (0.20%)	1 / 134 (0.75%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant melanoma in situ			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small cell lung cancer			
subjects affected / exposed	2 / 500 (0.40%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of lung			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of skin			

subjects affected / exposed	10 / 500 (2.00%)	5 / 134 (3.73%)	1 / 132 (0.76%)
occurrences causally related to treatment / all	0 / 12	0 / 6	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transitional cell carcinoma			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour flare			
subjects affected / exposed	2 / 500 (0.40%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	2 / 500 (0.40%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	2 / 500 (0.40%)	1 / 134 (0.75%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Superior vena cava syndrome			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	3 / 500 (0.60%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Death			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Generalised oedema			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Face oedema			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disease progression			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Impaired healing			
subjects affected / exposed	0 / 500 (0.00%)	0 / 134 (0.00%)	1 / 132 (0.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	3 / 500 (0.60%)	1 / 134 (0.75%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple organ dysfunction syndrome			

subjects affected / exposed	1 / 500 (0.20%)	1 / 134 (0.75%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Malaise			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	1 / 500 (0.20%)	3 / 134 (2.24%)	2 / 132 (1.52%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden death			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Contrast media allergy			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Contrast media reaction			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug hypersensitivity			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			

Uterine prolapse			
subjects affected / exposed	0 / 500 (0.00%)	1 / 134 (0.75%)	0 / 132 (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
Cystocele			
subjects affected / exposed	0 / 500 (0.00%)	1 / 134 (0.75%)	0 / 132 (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, thoracic and mediastinal disorders			
Aspiration			
subjects affected / exposed	2 / 500 (0.40%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	2 / 500 (0.40%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchial obstruction			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	3 / 500 (0.60%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cough			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	4 / 500 (0.80%)	0 / 134 (0.00%)	1 / 132 (0.76%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pulmonary embolism			
subjects affected / exposed	5 / 500 (1.00%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	8 / 500 (1.60%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 8	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	3 / 500 (0.60%)	1 / 134 (0.75%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Granulomatous pneumonitis			
subjects affected / exposed	0 / 500 (0.00%)	0 / 134 (0.00%)	1 / 132 (0.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleuritic pain			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary hypertension			
subjects affected / exposed	2 / 500 (0.40%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary oedema			
subjects affected / exposed	0 / 500 (0.00%)	1 / 134 (0.75%)	0 / 132 (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 acidosis			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory arrest			

subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Respiratory distress			
subjects affected / exposed	2 / 500 (0.40%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	3 / 500 (0.60%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 2	0 / 0	0 / 0
Psychiatric disorders			
Delirium			
subjects affected / exposed	0 / 500 (0.00%)	1 / 134 (0.75%)	0 / 132 (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
Mental status changes			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal ideation			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	0 / 500 (0.00%)	1 / 134 (0.75%)	0 / 132 (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
Depression			
subjects affected / exposed	0 / 500 (0.00%)	1 / 134 (0.75%)	0 / 132 (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
Product issues			

Device occlusion			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Anticoagulation drug level above therapeutic			
subjects affected / exposed	0 / 500 (0.00%)	0 / 134 (0.00%)	1 / 132 (0.76%)
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 bilirubin increased			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lipase increased			
subjects affected / exposed	0 / 500 (0.00%)	1 / 134 (0.75%)	0 / 132 (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
Troponin increased			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
White blood cell count decreased			
subjects affected / exposed	3 / 500 (0.60%)	1 / 134 (0.75%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Cervical vertebral fracture			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ankle fracture			

subjects affected / exposed	0 / 500 (0.00%)	0 / 134 (0.00%)	1 / 132 (0.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	0 / 500 (0.00%)	2 / 134 (1.49%)	0 / 132 (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
Lower limb fracture			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	1 / 132 (0.76%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infusion related reaction			
subjects affected / exposed	2 / 500 (0.40%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ilium fracture			
subjects affected / exposed	0 / 500 (0.00%)	1 / 134 (0.75%)	0 / 132 (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
Hip fracture			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Heat exhaustion			
subjects affected / exposed	0 / 500 (0.00%)	1 / 134 (0.75%)	0 / 132 (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
Post concussion syndrome			

subjects affected / exposed	0 / 500 (0.00%)	1 / 134 (0.75%)	0 / 132 (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
Tibia fracture			
subjects affected / exposed	0 / 500 (0.00%)	1 / 134 (0.75%)	0 / 132 (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 compression fracture			
subjects affected / exposed	0 / 500 (0.00%)	1 / 134 (0.75%)	0 / 132 (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
Scapula fracture			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	2 / 500 (0.40%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	2 / 500 (0.40%)	1 / 134 (0.75%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic valve incompetence			

subjects affected / exposed	0 / 500 (0.00%)	1 / 134 (0.75%)	0 / 132 (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
Atrial fibrillation			
subjects affected / exposed	9 / 500 (1.80%)	3 / 134 (2.24%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 9	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	0 / 500 (0.00%)	0 / 134 (0.00%)	1 / 132 (0.76%)
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 tachycardia			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular block			
subjects affected / exposed	0 / 500 (0.00%)	0 / 134 (0.00%)	1 / 132 (0.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bradycardia			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Trifascicular block			
subjects affected / exposed	0 / 500 (0.00%)	1 / 134 (0.75%)	0 / 132 (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
Myocardial infarction			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Extrasystoles			

subjects affected / exposed	0 / 500 (0.00%)	1 / 134 (0.75%)	0 / 132 (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
Cardio-respiratory arrest			
subjects affected / exposed	2 / 500 (0.40%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	1 / 132 (0.76%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	1 / 500 (0.20%)	1 / 134 (0.75%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	3 / 500 (0.60%)	1 / 134 (0.75%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ataxia			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bell's palsy			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral haemorrhage			
subjects affected / exposed	0 / 500 (0.00%)	0 / 134 (0.00%)	1 / 132 (0.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			

subjects affected / exposed	3 / 500 (0.60%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic cerebral infarction			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	2 / 500 (0.40%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lethargy			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 500 (0.00%)	1 / 134 (0.75%)	0 / 132 (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
Somnolence			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	2 / 500 (0.40%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalopathy			

subjects affected / exposed	0 / 500 (0.00%)	1 / 134 (0.75%)	0 / 132 (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	2 / 500 (0.40%)	1 / 134 (0.75%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient global amnesia			
subjects affected / exposed	0 / 500 (0.00%)	1 / 134 (0.75%)	0 / 132 (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
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	14 / 500 (2.80%)	1 / 134 (0.75%)	1 / 132 (0.76%)
occurrences causally related to treatment / all	0 / 15	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia			
subjects affected / exposed	8 / 500 (1.60%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 8	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			
subjects affected / exposed	0 / 500 (0.00%)	1 / 134 (0.75%)	0 / 132 (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
Neutropenia			
subjects affected / exposed	15 / 500 (3.00%)	3 / 134 (2.24%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 19	0 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	3 / 500 (0.60%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			

subjects affected / exposed	6 / 500 (1.20%)	1 / 134 (0.75%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 6	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Ear canal stenosis			
subjects affected / exposed	0 / 500 (0.00%)	0 / 134 (0.00%)	1 / 132 (0.76%)
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			
Visual impairment			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angle closure glaucoma			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	3 / 500 (0.60%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	5 / 500 (1.00%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	3 / 500 (0.60%)	2 / 134 (1.49%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Dysphagia			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epiploic appendagitis			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocolitis			
subjects affected / exposed	0 / 500 (0.00%)	1 / 134 (0.75%)	0 / 132 (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
Faecaloma			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obstruction gastric			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	2 / 500 (0.40%)	1 / 134 (0.75%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine polyp			
subjects affected / exposed	0 / 500 (0.00%)	1 / 134 (0.75%)	0 / 132 (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
Intestinal perforation			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			

subjects affected / exposed	2 / 500 (0.40%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer haemorrhage			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	3 / 500 (0.60%)	0 / 134 (0.00%)	1 / 132 (0.76%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Rectal haemorrhage			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 500 (0.00%)	1 / 134 (0.75%)	0 / 132 (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
Oesophageal spasm			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Volvulus of small bowel			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	2 / 500 (0.40%)	2 / 134 (1.49%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatic failure			

subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cholecystitis chronic			
subjects affected / exposed	0 / 500 (0.00%)	1 / 134 (0.75%)	0 / 132 (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
Bile duct stone			
subjects affected / exposed	0 / 500 (0.00%)	1 / 134 (0.75%)	0 / 132 (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
Cholecystitis			
subjects affected / exposed	1 / 500 (0.20%)	2 / 134 (1.49%)	1 / 132 (0.76%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic haematoma			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaundice			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertransaminasaemia			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Angioedema			

subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin ulcer			
subjects affected / exposed	2 / 500 (0.40%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug eruption			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	9 / 500 (1.80%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 10	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Urinary tract disorder			
subjects affected / exposed	0 / 500 (0.00%)	1 / 134 (0.75%)	0 / 132 (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	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic kidney disease			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract obstruction			

subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 500 (0.00%)	1 / 134 (0.75%)	1 / 132 (0.76%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	1 / 500 (0.20%)	1 / 134 (0.75%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Flank pain			
subjects affected / exposed	4 / 500 (0.80%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Costochondritis			
subjects affected / exposed	0 / 500 (0.00%)	1 / 134 (0.75%)	0 / 132 (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
Sacral pain			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rhabdomyolysis			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			

subjects affected / exposed	0 / 500 (0.00%)	2 / 134 (1.49%)	0 / 132 (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
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspergillus infection			
subjects affected / exposed	0 / 500 (0.00%)	1 / 134 (0.75%)	0 / 132 (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
Atypical pneumonia			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	0 / 500 (0.00%)	0 / 134 (0.00%)	1 / 132 (0.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronavirus infection			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile infection			
subjects affected / exposed	2 / 500 (0.40%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			

subjects affected / exposed	5 / 500 (1.00%)	3 / 134 (2.24%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Catheter site infection			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	1 / 500 (0.20%)	3 / 134 (2.24%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacteraemia			
subjects affected / exposed	1 / 500 (0.20%)	1 / 134 (0.75%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis C			
subjects affected / exposed	0 / 500 (0.00%)	0 / 134 (0.00%)	1 / 132 (0.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Groin abscess			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal viral infection			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			

subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epididymitis			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disseminated varicella zoster virus infection			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Histoplasmosis			
subjects affected / exposed	0 / 500 (0.00%)	1 / 134 (0.75%)	0 / 132 (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
Influenza			
subjects affected / exposed	2 / 500 (0.40%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint abscess			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	18 / 500 (3.60%)	8 / 134 (5.97%)	1 / 132 (0.76%)
occurrences causally related to treatment / all	0 / 20	0 / 11	0 / 2
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Peritonsillar abscess			

subjects affected / exposed	0 / 500 (0.00%)	0 / 134 (0.00%)	1 / 132 (0.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Periorbital cellulitis			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media			
subjects affected / exposed	0 / 500 (0.00%)	1 / 134 (0.75%)	0 / 132 (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
Osteomyelitis			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal candidiasis			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Localised infection			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Progressive multifocal leukoencephalopathy			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia viral			
subjects affected / exposed	0 / 500 (0.00%)	1 / 134 (0.75%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia streptococcal			

subjects affected / exposed	2 / 500 (0.40%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia mycoplasmal			
subjects affected / exposed	0 / 500 (0.00%)	1 / 134 (0.75%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia influenzal			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	3 / 500 (0.60%)	2 / 134 (1.49%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pseudomonas infection			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psoas abscess			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary sepsis			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection viral			

subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	7 / 500 (1.40%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 8	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	2 / 500 (0.40%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin infection			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Streptococcal sepsis			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 500 (0.00%)	2 / 134 (1.49%)	0 / 132 (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
Urinary tract infection			
subjects affected / exposed	3 / 500 (0.60%)	3 / 134 (2.24%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 8	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	2 / 500 (0.40%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Varicella			

subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyperuricaemia			
subjects affected / exposed	2 / 500 (0.40%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	8 / 500 (1.60%)	1 / 134 (0.75%)	1 / 132 (0.76%)
occurrences causally related to treatment / all	0 / 8	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Decreased appetite			
subjects affected / exposed	1 / 500 (0.20%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			
subjects affected / exposed	5 / 500 (1.00%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour lysis syndrome			
subjects affected / exposed	2 / 500 (0.40%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypovolaemia			
subjects affected / exposed	0 / 500 (0.00%)	0 / 134 (0.00%)	1 / 132 (0.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			

subjects affected / exposed	2 / 500 (0.40%)	1 / 134 (0.75%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	3 / 500 (0.60%)	1 / 134 (0.75%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Induction Period: Lenalidomide - Rituximab	Maintenance Period: Arm A	Maintenance Period: Arm B
Total subjects affected by non-serious adverse events			
subjects affected / exposed	491 / 500 (98.20%)	129 / 134 (96.27%)	106 / 132 (80.30%)
Vascular disorders			
Hypertension			
subjects affected / exposed	34 / 500 (6.80%)	9 / 134 (6.72%)	6 / 132 (4.55%)
occurrences (all)	41	17	6
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	50 / 500 (10.00%)	14 / 134 (10.45%)	5 / 132 (3.79%)
occurrences (all)	63	18	6
Oedema peripheral			
subjects affected / exposed	81 / 500 (16.20%)	14 / 134 (10.45%)	3 / 132 (2.27%)
occurrences (all)	89	14	4
Influenza like illness			
subjects affected / exposed	14 / 500 (2.80%)	7 / 134 (5.22%)	1 / 132 (0.76%)
occurrences (all)	18	8	1
Fatigue			
subjects affected / exposed	225 / 500 (45.00%)	27 / 134 (20.15%)	15 / 132 (11.36%)
occurrences (all)	252	35	17
Chills			
subjects affected / exposed	43 / 500 (8.60%)	5 / 134 (3.73%)	5 / 132 (3.79%)
occurrences (all)	47	8	5
Immune system disorders			

Hypogammaglobulinaemia			
subjects affected / exposed	8 / 500 (1.60%)	7 / 134 (5.22%)	2 / 132 (1.52%)
occurrences (all)	8	9	2
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	103 / 500 (20.60%)	41 / 134 (30.60%)	20 / 132 (15.15%)
occurrences (all)	128	52	21
Dyspnoea			
subjects affected / exposed	73 / 500 (14.60%)	18 / 134 (13.43%)	2 / 132 (1.52%)
occurrences (all)	79	23	2
Nasal congestion			
subjects affected / exposed	23 / 500 (4.60%)	10 / 134 (7.46%)	2 / 132 (1.52%)
occurrences (all)	25	11	2
Oropharyngeal pain			
subjects affected / exposed	37 / 500 (7.40%)	9 / 134 (6.72%)	2 / 132 (1.52%)
occurrences (all)	43	9	2
Respiratory tract congestion			
subjects affected / exposed	3 / 500 (0.60%)	8 / 134 (5.97%)	1 / 132 (0.76%)
occurrences (all)	3	8	1
Sinus congestion			
subjects affected / exposed	19 / 500 (3.80%)	7 / 134 (5.22%)	1 / 132 (0.76%)
occurrences (all)	22	9	1
Upper-airway cough syndrome			
subjects affected / exposed	21 / 500 (4.20%)	10 / 134 (7.46%)	4 / 132 (3.03%)
occurrences (all)	22	12	4
Psychiatric disorders			
Anxiety			
subjects affected / exposed	31 / 500 (6.20%)	8 / 134 (5.97%)	3 / 132 (2.27%)
occurrences (all)	36	10	3
Insomnia			
subjects affected / exposed	50 / 500 (10.00%)	7 / 134 (5.22%)	5 / 132 (3.79%)
occurrences (all)	50	7	5
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	30 / 500 (6.00%)	5 / 134 (3.73%)	2 / 132 (1.52%)
occurrences (all)	36	15	2

Aspartate aminotransferase increased			
subjects affected / exposed	22 / 500 (4.40%)	7 / 134 (5.22%)	4 / 132 (3.03%)
occurrences (all)	28	18	4
Blood creatinine increased			
subjects affected / exposed	22 / 500 (4.40%)	12 / 134 (8.96%)	4 / 132 (3.03%)
occurrences (all)	27	24	4
Lymphocyte count decreased			
subjects affected / exposed	11 / 500 (2.20%)	7 / 134 (5.22%)	3 / 132 (2.27%)
occurrences (all)	14	12	3
Weight decreased			
subjects affected / exposed	34 / 500 (6.80%)	14 / 134 (10.45%)	4 / 132 (3.03%)
occurrences (all)	34	15	4
White blood cell count decreased			
subjects affected / exposed	20 / 500 (4.00%)	10 / 134 (7.46%)	1 / 132 (0.76%)
occurrences (all)	34	24	1
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	24 / 500 (4.80%)	13 / 134 (9.70%)	7 / 132 (5.30%)
occurrences (all)	31	19	7
Infusion related reaction			
subjects affected / exposed	53 / 500 (10.60%)	0 / 134 (0.00%)	0 / 132 (0.00%)
occurrences (all)	58	0	0
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	30 / 500 (6.00%)	3 / 134 (2.24%)	0 / 132 (0.00%)
occurrences (all)	31	3	0
Headache			
subjects affected / exposed	66 / 500 (13.20%)	15 / 134 (11.19%)	11 / 132 (8.33%)
occurrences (all)	76	22	13
Peripheral sensory neuropathy			
subjects affected / exposed	56 / 500 (11.20%)	14 / 134 (10.45%)	6 / 132 (4.55%)
occurrences (all)	60	17	6
Dizziness			
subjects affected / exposed	68 / 500 (13.60%)	14 / 134 (10.45%)	7 / 132 (5.30%)
occurrences (all)	71	18	7
Blood and lymphatic system disorders			

Thrombocytopenia			
subjects affected / exposed	74 / 500 (14.80%)	9 / 134 (6.72%)	5 / 132 (3.79%)
occurrences (all)	106	18	8
Neutropenia			
subjects affected / exposed	217 / 500 (43.40%)	54 / 134 (40.30%)	22 / 132 (16.67%)
occurrences (all)	520	168	32
Lymphopenia			
subjects affected / exposed	33 / 500 (6.60%)	5 / 134 (3.73%)	3 / 132 (2.27%)
occurrences (all)	45	12	3
Anaemia			
subjects affected / exposed	77 / 500 (15.40%)	12 / 134 (8.96%)	8 / 132 (6.06%)
occurrences (all)	112	23	11
Leukopenia			
subjects affected / exposed	67 / 500 (13.40%)	13 / 134 (9.70%)	9 / 132 (6.82%)
occurrences (all)	113	30	16
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	5 / 500 (1.00%)	7 / 134 (5.22%)	3 / 132 (2.27%)
occurrences (all)	5	9	3
Eye disorders			
Vision blurred			
subjects affected / exposed	18 / 500 (3.60%)	9 / 134 (6.72%)	0 / 132 (0.00%)
occurrences (all)	19	9	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	57 / 500 (11.40%)	13 / 134 (9.70%)	8 / 132 (6.06%)
occurrences (all)	72	20	8
Stomatitis			
subjects affected / exposed	37 / 500 (7.40%)	3 / 134 (2.24%)	3 / 132 (2.27%)
occurrences (all)	41	3	3
Nausea			
subjects affected / exposed	150 / 500 (30.00%)	15 / 134 (11.19%)	6 / 132 (4.55%)
occurrences (all)	189	23	6
Dyspepsia			
subjects affected / exposed	35 / 500 (7.00%)	4 / 134 (2.99%)	0 / 132 (0.00%)
occurrences (all)	38	4	0
Dry mouth			

subjects affected / exposed	31 / 500 (6.20%)	0 / 134 (0.00%)	1 / 132 (0.76%)
occurrences (all)	31	0	1
Diarrhoea			
subjects affected / exposed	176 / 500 (35.20%)	56 / 134 (41.79%)	11 / 132 (8.33%)
occurrences (all)	262	90	13
Constipation			
subjects affected / exposed	146 / 500 (29.20%)	12 / 134 (8.96%)	2 / 132 (1.52%)
occurrences (all)	161	16	2
Vomiting			
subjects affected / exposed	54 / 500 (10.80%)	10 / 134 (7.46%)	4 / 132 (3.03%)
occurrences (all)	64	14	4
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	41 / 500 (8.20%)	4 / 134 (2.99%)	2 / 132 (1.52%)
occurrences (all)	44	4	2
Night sweats			
subjects affected / exposed	39 / 500 (7.80%)	8 / 134 (5.97%)	6 / 132 (4.55%)
occurrences (all)	46	10	6
Pruritus			
subjects affected / exposed	96 / 500 (19.20%)	2 / 134 (1.49%)	3 / 132 (2.27%)
occurrences (all)	107	2	3
Rash			
subjects affected / exposed	33 / 500 (6.60%)	0 / 134 (0.00%)	2 / 132 (1.52%)
occurrences (all)	38	0	2
Rash maculo-papular			
subjects affected / exposed	82 / 500 (16.40%)	6 / 134 (4.48%)	1 / 132 (0.76%)
occurrences (all)	107	11	1
Rash pruritic			
subjects affected / exposed	30 / 500 (6.00%)	6 / 134 (4.48%)	2 / 132 (1.52%)
occurrences (all)	32	7	2
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	14 / 500 (2.80%)	7 / 134 (5.22%)	4 / 132 (3.03%)
occurrences (all)	14	7	4
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	68 / 500 (13.60%)	23 / 134 (17.16%)	18 / 132 (13.64%)
occurrences (all)	76	26	18
Back pain			
subjects affected / exposed	57 / 500 (11.40%)	9 / 134 (6.72%)	4 / 132 (3.03%)
occurrences (all)	64	9	4
Muscle spasms			
subjects affected / exposed	64 / 500 (12.80%)	11 / 134 (8.21%)	3 / 132 (2.27%)
occurrences (all)	74	14	3
Myalgia			
subjects affected / exposed	31 / 500 (6.20%)	8 / 134 (5.97%)	2 / 132 (1.52%)
occurrences (all)	32	10	2
Neck pain			
subjects affected / exposed	25 / 500 (5.00%)	10 / 134 (7.46%)	2 / 132 (1.52%)
occurrences (all)	28	12	2
Pain in extremity			
subjects affected / exposed	37 / 500 (7.40%)	11 / 134 (8.21%)	9 / 132 (6.82%)
occurrences (all)	39	12	9
Infections and infestations			
Bronchitis			
subjects affected / exposed	23 / 500 (4.60%)	12 / 134 (8.96%)	5 / 132 (3.79%)
occurrences (all)	29	14	6
COVID-19			
subjects affected / exposed	0 / 500 (0.00%)	8 / 134 (5.97%)	0 / 132 (0.00%)
occurrences (all)	0	9	0
Nasopharyngitis			
subjects affected / exposed	26 / 500 (5.20%)	5 / 134 (3.73%)	3 / 132 (2.27%)
occurrences (all)	30	5	3
Pneumonia			
subjects affected / exposed	35 / 500 (7.00%)	17 / 134 (12.69%)	5 / 132 (3.79%)
occurrences (all)	41	22	5
Urinary tract infection			
subjects affected / exposed	41 / 500 (8.20%)	11 / 134 (8.21%)	4 / 132 (3.03%)
occurrences (all)	64	27	4
Upper respiratory tract infection			

subjects affected / exposed	65 / 500 (13.00%)	22 / 134 (16.42%)	14 / 132 (10.61%)
occurrences (all)	89	34	15
Sinusitis			
subjects affected / exposed	43 / 500 (8.60%)	16 / 134 (11.94%)	11 / 132 (8.33%)
occurrences (all)	53	21	18
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	69 / 500 (13.80%)	8 / 134 (5.97%)	3 / 132 (2.27%)
occurrences (all)	74	9	4
Hyperglycaemia			
subjects affected / exposed	24 / 500 (4.80%)	8 / 134 (5.97%)	3 / 132 (2.27%)
occurrences (all)	33	14	3
Hyperuricaemia			
subjects affected / exposed	17 / 500 (3.40%)	8 / 134 (5.97%)	7 / 132 (5.30%)
occurrences (all)	24	12	12
Hypokalaemia			
subjects affected / exposed	63 / 500 (12.60%)	16 / 134 (11.94%)	8 / 132 (6.06%)
occurrences (all)	110	47	11
Hypophosphataemia			
subjects affected / exposed	27 / 500 (5.40%)	6 / 134 (4.48%)	7 / 132 (5.30%)
occurrences (all)	36	11	11

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 January 2014	Addition of Overall Survival as a secondary endpoint; Changes in the pregnancy restriction language to reflect the Rituximab Prescribing information.
24 February 2015	Modification of Randomization Timepoint; Modification of Inclusion/Exclusion Criteria; Lenalidomide monotherapy maintenance changed to optional; Revision to Secondary Endpoints and Interim Analyses.
27 August 2019	A protocol addendum dated 22 Jun 2017 was issued to address aspects of the protocol that are adapted in order to comply with laws and drug regulations applicable in Germany. These changes are now incorporated in the current global protocol amendment.
03 November 2020	Considering the current progression free survival (PFS) event rate, which is slower than originally predicted (approximately 60 PFS events as of August 2020), the challenging follow-up of subjects in the context of the COVID-19 pandemic, and estimated timing of final analysis, one nonbinding interim analysis for patients in the maintenance phase is planned at 50% of information (95 PFS events) for both superiority and futility. This analysis will enhance formal benefit/risk assessment for subjects continuing on treatment. The date of occurrence of the 95th PFS event will be used as data cut-off date for the analysis. This interim analysis will be conducted by an external independent statistician, while the study team will remain blinded. The study may be stopped early for futility if the observed hazard ratio (HR) is > 1.154, based on Gamma (-8) family (Hwang, Shih, and DeCani, 1990), ie, in favor of the control arm, and/or if recommended by the data monitoring committee (DMC) based on the safety profile of this combination regimen. The stopping boundary for superiority based on O'Brien Fleming Analog (Lan & DeMets, 1983) is hazard ratio ≤ 0.546, if the observed HR cross the superiority boundary in favor of the proposed treatment, the trial may stop and claim the superiority, reflecting a one-sided p-value < 0.002. The stopping rule for superiority will occur if the observed hazard ratio HR is ≤ 0.54.
11 September 2022	Updated company name and contact; This analysis has been updated due to the number of subjects that have been censored, it is no longer feasible to meet the number of PFS events required; Updated study duration period; Added that upon confirmation of 114 PFS events, subjects will be followed annually (± 4 weeks).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported