



Clinical trial results:

A Phase 3, Randomized Study to Assess the Efficacy and Safety of Ublituximab in Combination with TGR-1202 (Umbralisib) Compared to Obinutuzumab in Combination with Chlorambucil in Patients with Chronic Lymphocytic Leukemia (CLL)

Summary

EudraCT number	2015-005758-36
Trial protocol	PL BG ES GB IT
Global end of trial date	22 February 2023

Results information

Result version number	v1 (current)
This version publication date	20 March 2024
First version publication date	20 March 2024

Trial information

Trial identification

Sponsor protocol code	UTX-TGR-304
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02612311
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	TG Therapeutics
Sponsor organisation address	2 Gansevoort Street, 9 Floor, New York, United States, 10014
Public contact	Izabela Kozdraś-Urbaneck, Brilliance Sp. z o.o., +48 668 166 876, clinicalsupport@tgtxinc.com
Scientific contact	Izabela Kozdraś-Urbaneck, Brilliance Sp. z o.o., 8775758489 668 166 876, clinicalsupport@tgtxinc.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	22 February 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 February 2023
Global end of trial reached?	Yes
Global end of trial date	22 February 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To establish that the combination of ublituximab + umbralisib is superior to the combination of obinutuzumab + chlorambucil as measured by Progression-Free Survival (PFS) in subjects with CLL

Protection of trial subjects:

This study was conducted in accordance with the protocol and consensus ethical principles originating in or derived from the Declaration of Helsinki and in compliance with all ICH GCP Guidelines. The Investigator or his/her representative explained the nature of the study to the subject or his/her legally authorized representative and answered all questions regarding the study. Subjects and/or their legally authorized representative were informed that their participation was voluntary. Subjects or their legally authorized representative were required to sign a statement of informed consent that met the requirements of 21 CFR 50, local regulations, ICH guidelines, HIPAA requirements, where applicable, and the IRB/IEC or study center. Investigative sites were instructed to obtain written informed consent before the subject was enrolled in the study and document the date the written consent was obtained. The authorized person obtaining the informed consent was also instructed to sign the ICF.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 November 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 397
Country: Number of subjects enrolled	Israel: 15
Country: Number of subjects enrolled	United Kingdom: 25
Country: Number of subjects enrolled	Russian Federation: 27
Country: Number of subjects enrolled	Poland: 126
Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	Italy: 12
Worldwide total number of subjects	603
EEA total number of subjects	139

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)	234
From 65 to 84 years	349
85 years and over	20

Subject disposition

Recruitment

Recruitment details:

A total of 603 subjects were enrolled randomised and treated in the study. Of which, none of the subjects completed the study.

Pre-assignment

Screening details:

Subjects took part in the study at multiple investigative sites in the United States, Israel, Italy, Poland, Russian Federation, Spain and the United Kingdom from 19 November 2015 to 22 February 2023.

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	Arm A: Ublituximab + Umbralisib

Arm description:

Subjects received ublituximab, 150 milligrams (mg), intravenously (IV), on Day 1, 750 mg on Day 2, followed by 900 mg on Days 8 and 15 of Cycle 1 (cycle length=28 days), Day 1 of Cycles 2-6, and once every 3 cycles thereafter, along with umbralisib, 800 mg, orally, once daily during each cycle until disease progression, lack of tolerability, or until the treatment is commercially available or up to 87 months.

Arm type	Experimental
Investigational medicinal product name	Ublituximab
Investigational medicinal product code	
Other name	TG-1101
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Ublituximab, 900 mg, was administered as IV infusion

Investigational medicinal product name	Umbralisib
Investigational medicinal product code	
Other name	TGR-1202
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Umbralisib, 800 mg, tablet was administered orally

Arm title	Arm B: Obinutuzumab + Chlorambucil
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Arm description:

Subjects received Obinutuzumab 100 mg, IV on Day 1, 900 mg on Day 2, followed by 1000 mg on Days 8 and 15 of cycle 1 (cycle length = 28 days), Day 1 of Cycle 2-6 along with Chlorambucil 0.5 milligram per kilogram (mg/kg) tablet orally on Days 1 and 15 once daily during each cycle until disease progression, lack of tolerability, or until the treatment is commercially available or up to 87 months.

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

Dosage and administration details:	
Obinutuzumab, 100 mg, was administered as IV infusion	
Investigational medicinal product name	Chlorambucil
Investigational medicinal product code	
Other name	Leukeran
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Chlorambucil, 0.5 mg/kg, tablet was administered orally	
Arm title	Arm C: Ublituximab
Arm description:	
Subjects received ublituximab, 150 mg, IV, on Day 1, 750 mg on Day 2, followed by 900 mg on Days 8 and 15 of Cycle 1 (cycle length=28 days), Day 1 of Cycles 2-6, and once every 3 cycles thereafter, until disease progression, lack of tolerability, or until the treatment is commercially available or up to 87 months.	
Arm type	Experimental
Investigational medicinal product name	Ublituximab
Investigational medicinal product code	
Other name	TG-1101
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use
Dosage and administration details:	
Ublituximab, 900 mg, was administered as IV infusion	
Arm title	Arm D: Umbralisib
Arm description:	
Subjects received umbralisib, 800 mg tablets, orally, once daily during each cycle (cycle length= 28 days) until removal from study or up to 87 months.	
Arm type	Experimental
Investigational medicinal product name	Umbralisib
Investigational medicinal product code	
Other name	TGR-1202
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details:	
Umbralisib, 800 mg, tablet was administered orally	

Number of subjects in period 1	Arm A: Ublituximab + Umbralisib	Arm B: Obinutuzumab + Chlorambucil	Arm C: Ublituximab
Started	210	211	91
Completed	0	0	0
Not completed	210	211	91
Lack of Efficacy	-	-	-
Adverse Event	16	12	7
Initiation of non-protocol intervention	5	3	-
Reason Not Specified	3	7	4
Progressive Disease confirmed by central radiology	75	113	38

Investigator Decision	11	15	6
Site Terminated by Sponsor	29	12	13
Withdrawal of Consent by Subject	29	24	6
Death	29	10	11
Lost to Follow-up	2	2	1
Unknown/missing	10	13	4
Non-Compliance with Study	1	-	-
Lack of efficacy	-	-	1

Number of subjects in period 1	Arm D: Umbralisib
Started	91
Completed	0
Not completed	91
Lack of Efficacy	1
Adverse Event	13
Initiation of non-protocol intervention	-
Reason Not Specified	5
Progressive Disease confirmed by central radiology	43
Investigator Decision	6
Site Terminated by Sponsor	5
Withdrawal of Consent by Subject	5
Death	11
Lost to Follow-up	2
Unknown/missing	-
Non-Compliance with Study	-
Lack of efficacy	-

Baseline characteristics

Reporting groups

Reporting group title	Arm A: Ublituximab + Umbralisib
Reporting group description:	
Subjects received ublituximab, 150 milligrams (mg), intravenously (IV), on Day 1, 750 mg on Day 2, followed by 900 mg on Days 8 and 15 of Cycle 1 (cycle length=28 days), Day 1 of Cycles 2-6, and once every 3 cycles thereafter, along with umbralisib, 800 mg, orally, once daily during each cycle until disease progression, lack of tolerability, or until the treatment is commercially available or up to 87 months.	
Reporting group title	Arm B: Obinutuzumab + Chlorambucil
Reporting group description:	
Subjects received Obinutuzumab 100 mg, IV on Day 1, 900 mg on Day 2, followed by 1000 mg on Days 8 and 15 of cycle 1 (cycle length = 28 days), Day 1 of Cycle 2-6 along with Chlorambucil 0.5 milligram per kilogram (mg/kg) tablet orally on Days 1 and 15 once daily during each cycle until disease progression, lack of tolerability, or until the treatment is commercially available or up to 87 months.	
Reporting group title	Arm C: Ublituximab
Reporting group description:	
Subjects received ublituximab, 150 mg, IV, on Day 1, 750 mg on Day 2, followed by 900 mg on Days 8 and 15 of Cycle 1 (cycle length=28 days), Day 1 of Cycles 2-6, and once every 3 cycles thereafter, until disease progression, lack of tolerability, or until the treatment is commercially available or up to 87 months.	
Reporting group title	Arm D: Umbralisib
Reporting group description:	
Subjects received umbralisib, 800 mg tablets, orally, once daily during each cycle (cycle length= 28 days) until removal from study or up to 87 months.	

Reporting group values	Arm A: Ublituximab + Umbralisib	Arm B: Obinutuzumab + Chlorambucil	Arm C: Ublituximab
Number of subjects	210	211	91
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean full range (min-max)	66.2 39 to 88	67.1 36 to 91	67.6 40 to 88
Gender categorical Units: Subjects			
Female	75	67	23
Male	135	144	68
Ethnicity Units: Subjects			
Hispanic or Latino	3	5	2
Not Hispanic or Latino	193	194	86
Unknown or Not Reported	14	12	3
Race Units: Subjects			
American Indian or Alaska Native	0	1	0
Asian	0	1	1
Black or African American	9	6	5

Native Hawaiian or Other Pacific Islander	1	0	0
White	189	195	83
Multiple	2	0	0
Other	1	1	0
Not Reported	8	7	2

Reporting group values	Arm D: Umbralisib	Total	
Number of subjects	91	603	
Age categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	66.3		
full range (min-max)	43 to 86	-	
Gender categorical			
Units: Subjects			
Female	30	195	
Male	61	408	
Ethnicity			
Units: Subjects			
Hispanic or Latino	3	13	
Not Hispanic or Latino	83	556	
Unknown or Not Reported	5	34	
Race			
Units: Subjects			
American Indian or Alaska Native	0	1	
Asian	1	3	
Black or African American	5	25	
Native Hawaiian or Other Pacific Islander	0	1	
White	82	549	
Multiple	0	2	
Other	2	4	
Not Reported	1	18	

End points

End points reporting groups

Reporting group title	Arm A: Ublituximab + Umbralisib
Reporting group description: Subjects received ublituximab, 150 milligrams (mg), intravenously (IV), on Day 1, 750 mg on Day 2, followed by 900 mg on Days 8 and 15 of Cycle 1 (cycle length=28 days), Day 1 of Cycles 2-6, and once every 3 cycles thereafter, along with umbralisib, 800 mg, orally, once daily during each cycle until disease progression, lack of tolerability, or until the treatment is commercially available or up to 87 months.	
Reporting group title	Arm B: Obinutuzumab + Chlorambucil
Reporting group description: Subjects received Obinutuzumab 100 mg, IV on Day 1, 900 mg on Day 2, followed by 1000 mg on Days 8 and 15 of cycle 1 (cycle length = 28 days), Day 1 of Cycle 2-6 along with Chlorambucil 0.5 milligram per kilogram (mg/kg) tablet orally on Days 1 and 15 once daily during each cycle until disease progression, lack of tolerability, or until the treatment is commercially available or up to 87 months.	
Reporting group title	Arm C: Ublituximab
Reporting group description: Subjects received ublituximab, 150 mg, IV, on Day 1, 750 mg on Day 2, followed by 900 mg on Days 8 and 15 of Cycle 1 (cycle length=28 days), Day 1 of Cycles 2-6, and once every 3 cycles thereafter, until disease progression, lack of tolerability, or until the treatment is commercially available or up to 87 months.	
Reporting group title	Arm D: Umbralisib
Reporting group description: Subjects received umbralisib, 800 mg tablets, orally, once daily during each cycle (cycle length= 28 days) until removal from study or up to 87 months.	

Primary: Progression-Free Survival (PFS) Per International Workshop on Chronic Lymphocytic Leukemia (iwCLL) Criteria

End point title	Progression-Free Survival (PFS) Per International Workshop on Chronic Lymphocytic Leukemia (iwCLL) Criteria ^[1]
End point description: PFS was defined as the interval from enrollment to the earlier of the first documentation of definitive disease progression (PD) or death from any cause. PD was appearance of new nodes >1.5 centimetres (cm) in the longest diameter (LD) and >1.0 in longest perpendicular diameter (LPD), new or recurrent hepatomegaly or splenomegaly, new or reappearance of an unequivocal extra-nodal lesion, ≥50% increase from the nadir in the sum of products of diameters (SPD) of target lesions, ≥50% increase in the LD of an individual node or extra-nodal mass, splenic/hepatic enlargement of ≥50% from nadir, unequivocal increase in the size of non-target disease, transformation to a more aggressive histology, decrease in platelet count or Hgb, >50% decrease from the highest on-study platelet count, >20 grams per Liter (g/L) decrease from the highest on-study hemoglobin (Hgb).	
End point type	Primary
End point timeframe: Up to 87 months	

Notes:

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

Justification: Only descriptive analysis was conducted for the end point.

End point values	Arm A: Ublituximab + Umbralisib	Arm B: Obinutuzumab + Chlorambucil	Arm C: Ublituximab	Arm D: Umbralisib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	210	211	91	91
Units: Months				
median (confidence interval 95%)	33.2 (27.7 to 39.6)	17.5 (16.6 to 22.6)	32.9 (19.1 to 45.0)	22.4 (17.2 to 34.7)

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Response Rate (ORR) Per iwCLL Criteria

End point title	Overall Response Rate (ORR) Per iwCLL Criteria
End point description:	
<p>ORR=percent of subjects who achieve CR, CR with incomplete marrow recovery (CRi), partial response (PR) or nodular PR (nPR).CR: No evidence of new disease; Absolute lymphocyte count(ALC)<4x10⁹/liter(L);Regression of all target nodal masses to ≤1.5cm in LD;Normal spleen,liver size;Regression to normal of all nodal non-target disease and disappearance of all detectable;Non-nodal,non-target disease;Morphologically negative bone marrow;No lymphoid nodules;ANC >1.5x10⁹/L,platelets≥100x10⁹/L,Hgb≥110 g/L.PR:No evidence of new disease; Response in 2 of following if abnormal at baseline: ALC<4x10⁹/L or ≥50% decrease from baseline in sum of products of target nodal lesions;splenomegaly; hepatomegaly;≥50% decrease from baseline in CLL marrow infiltrate/B-lymphoid nodules;response in any 1: ANC>1.5x10⁹/L platelets>100x10⁹/L,Hgb>110g/L or ≥50% increase over baseline in any of these.CRi: for CR except with ANC<1000/μL and/or platelets<100. ITT population. Percentages are rounded off.</p>	
End point type	Secondary
End point timeframe:	
Up to 87 months	

End point values	Arm A: Ublituximab + Umbralisib	Arm B: Obinutuzumab + Chlorambucil	Arm C: Ublituximab	Arm D: Umbralisib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	210	211	91	91
Units: percentage of subjects				
number (not applicable)	83.3	68.7	42.9	61.5

Statistical analyses

No statistical analyses for this end point

Secondary: Complete Response (CR) Rate

End point title	Complete Response (CR) Rate
End point description:	
<p>The CR rate is defined as the percentage of subjects with a best overall response of complete response (CR) or complete response with incomplete marrow recovery (CRi). CR: No evidence of new disease; Absolute lymphocyte count(ALC)<4x10⁹/L; Regression of all target nodal masses to ≤1.5 cm in LD;</p>	

Normal spleen,liver size; Regression to normal of all nodal non-target disease and disappearance of all detectable; Non-nodal, non-target disease; Morphologically negative bone marrow; No lymphoid nodules; ANC>1.5x10⁹/L,platelets≥100x10⁹/L,hemoglobin (Hgb)≥110 g/L. CRi was as for CR except with ANC <1000/μL and/or platelets <100,000/μL. The ITT population included all randomised subjects, regardless of administration of study treatment (ublituximab, TGR-1202, obinutuzumab + chlorambucil, or ublituximab + TGR-1202). Percentages are rounded off to the nearest decimal point.

End point type	Secondary
End point timeframe:	
Up to 87 months	

End point values	Arm A: Ublituximab + Umbralisib	Arm B: Obinutuzumab + Chlorambucil	Arm C: Ublituximab	Arm D: Umbralisib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	210	211	91	91
Units: percentage of subjects				
number (not applicable)	5.7	1.4	3.3	0

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 defined as the interval from the first documentation of CR, CRi, PR, or nPR to the earlier of the first documentation of definitive disease progression or death from any cause.	
End point type	Secondary
End point timeframe:	
From first documentation of response to study treatment till disease progression/death (up to approximately 87 months)	

End point values	Arm A: Ublituximab + Umbralisib	Arm B: Obinutuzumab + Chlorambucil	Arm C: Ublituximab	Arm D: Umbralisib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	175	145	39	56
Units: months				
median (confidence interval 95%)	32.9 (27.8 to 39.4)	21.9 (14.6 to 26.6)	47.5 (40.3 to 57.8)	29.3 (17.1 to 36.5)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Experiencing at Least One Treatment-Emergent Adverse Event (TEAE)

End point title	Number of Subjects Experiencing at Least One Treatment-Emergent Adverse Event (TEAE)
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End point description:

An adverse event (AE) is any untoward medical occurrence in a subject or clinical investigation subject administered a pharmaceutical product. An AE does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporarily associated with the use of a medicinal product, whether or not considered related to the medicinal product. TEAE is any AE that occur after first dosing of study medication and through the end of the study or through 30 days after the last dose of study treatment, or is considered treatment-related regardless of the start date of the event, or is present before first dosing of study medication but worsens in intensity or the investigator subsequently considers treatment-related.

End point type	Secondary
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End point timeframe:

From first dose of study treatment up to end of study (up to approximately 87 months)

End point values	Arm A: Ublituximab + Umbralisib	Arm B: Obinutuzumab + Chlorambucil	Arm C: Ublituximab	Arm D: Umbralisib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	206	200	91	86
Units: count of subjects	205	195	88	86

Statistical analyses

No statistical analyses for this end point

Secondary: Minimal Residual Disease (MRD) Negativity Rate

End point title	Minimal Residual Disease (MRD) Negativity Rate
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End point description:

MRD negativity rate is defined as the percentage of subjects who are MRD negative. If a subject was determined to be MRD negative by peripheral blood, a bone marrow aspirate was obtained to assess MRD in the bone marrow. ITT population included all randomised subjects, regardless of administration of study treatment (ublituximab, TGR-1202, obinutuzumab + chlorambucil, or ublituximab + TGR-1202). Percentages are rounded off to the nearest decimal point.

End point type	Secondary
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End point timeframe:

From Cycle 6 until Cycle 15 (cycle length=28 days) up to approximately 81.5 months

End point values	Arm A: Ublituximab + Umbralisib	Arm B: Obinutuzumab + Chlorambucil	Arm C: Ublituximab	Arm D: Umbralisib
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	210	211	91	91
Units: percentage of subjects				
number (not applicable)	29.0	34.6	36.3	5.5

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study treatment up to end of study (up to approximately 87 months)

Adverse event reporting additional description:

The safety population included all randomized subjects who had received at least one dose of study treatment (ublituximab, TGR-1202, obinutuzumab + chlorambucil, or ublituximab + TGR-1202).

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	23.0
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Reporting groups

Reporting group title	Arm A: Ublituximab + Umbralisib
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Reporting group description:

Subjects received ublituximab, 150 milligrams (mg), intravenously (IV), on Day 1, 750 mg on Day 2, followed by 900 mg on Days 8 and 15 of Cycle 1 (cycle length=28 days), Day 1 of Cycles 2-6, and once every 3 cycles thereafter, along with umbralisib, 800 mg, orally, once daily during each cycle until disease progression, lack of tolerability, or until the treatment is commercially available or up to 87 months.

Reporting group title	Arm B: Obinutuzumab + Chlorambucil
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Reporting group description:

Subjects received Obinutuzumab 100 mg, IV on Day 1, 900 mg on Day 2, followed by 1000 mg on Days 8 and 15 of cycle 1 (cycle length = 28 days), Day 1 of Cycle 2-6 along with Chlorambucil 0.5 milligram per kilogram (mg/kg) tablet orally on Days 1 and 15 once daily during each cycle until disease progression, lack of tolerability, or until the treatment is commercially available or up to 87 months.

Reporting group title	Arm C: Ublituximab
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Reporting group description:

Subjects received ublituximab, 150 mg, IV, on Day 1, 750 mg on Day 2, followed by 900 mg on Days 8 and 15 of Cycle 1 (cycle length=28 days), Day 1 of Cycles 2-6, and once every 3 cycles thereafter, until disease progression, lack of tolerability, or until the treatment is commercially available or up to 87 months.

Reporting group title	Arm D: Umbralisib
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Reporting group description:

Subjects received umbralisib, 800 mg tablets, orally, once daily during each cycle (cycle length= 28 days) until removal from study or up to 87 months.

Serious adverse events	Arm A: Ublituximab + Umbralisib	Arm B: Obinutuzumab + Chlorambucil	Arm C: Ublituximab
Total subjects affected by serious adverse events			
subjects affected / exposed	118 / 206 (57.28%)	47 / 200 (23.50%)	33 / 91 (36.26%)
number of deaths (all causes)	82	40	25
number of deaths resulting from adverse events	3	1	2
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			

subjects affected / exposed	3 / 206 (1.46%)	1 / 200 (0.50%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of skin			
subjects affected / exposed	3 / 206 (1.46%)	0 / 200 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant melanoma			
subjects affected / exposed	2 / 206 (0.97%)	0 / 200 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma			
subjects affected / exposed	2 / 206 (0.97%)	0 / 200 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adenocarcinoma			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (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
Astrocytoma			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (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 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (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
Glioblastoma			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (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
Lung adenocarcinoma			

subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (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
Neoplasm malignant			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (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
Prostate cancer			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of head and neck			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (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 lung			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (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
Adenocarcinoma pancreas			
subjects affected / exposed	0 / 206 (0.00%)	0 / 200 (0.00%)	0 / 91 (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
Brain neoplasm			
subjects affected / exposed	0 / 206 (0.00%)	0 / 200 (0.00%)	0 / 91 (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
Clear cell renal cell carcinoma			
subjects affected / exposed	0 / 206 (0.00%)	0 / 200 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung neoplasm malignant			

subjects affected / exposed	0 / 206 (0.00%)	0 / 200 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to central nervous system			
subjects affected / exposed	0 / 206 (0.00%)	0 / 200 (0.00%)	0 / 91 (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
Neuroendocrine carcinoma of the skin			
subjects affected / exposed	0 / 206 (0.00%)	1 / 200 (0.50%)	0 / 91 (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
Plasma cell myeloma			
subjects affected / exposed	0 / 206 (0.00%)	0 / 200 (0.00%)	0 / 91 (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
Vascular disorders			
Aortic aneurysm			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (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
Peripheral vascular disorder			
subjects affected / exposed	1 / 206 (0.49%)	1 / 200 (0.50%)	0 / 91 (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
Hypertensive crisis			
subjects affected / exposed	0 / 206 (0.00%)	0 / 200 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orthostatic hypotension			
subjects affected / exposed	0 / 206 (0.00%)	0 / 200 (0.00%)	0 / 91 (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
Vascular compression			

subjects affected / exposed	0 / 206 (0.00%)	0 / 200 (0.00%)	0 / 91 (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
General disorders and administration site conditions			
Death			
subjects affected / exposed	3 / 206 (1.46%)	1 / 200 (0.50%)	2 / 91 (2.20%)
occurrences causally related to treatment / all	0 / 3	1 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Pyrexia			
subjects affected / exposed	2 / 206 (0.97%)	3 / 200 (1.50%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	1 / 2	2 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden cardiac death			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Systemic inflammatory response syndrome			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (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
Adverse drug reaction			
subjects affected / exposed	0 / 206 (0.00%)	1 / 200 (0.50%)	0 / 91 (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
Asthenia			
subjects affected / exposed	0 / 206 (0.00%)	0 / 200 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mucosal inflammation			

subjects affected / exposed	0 / 206 (0.00%)	0 / 200 (0.00%)	0 / 91 (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
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 206 (0.00%)	0 / 200 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Sudden death			
subjects affected / exposed	0 / 206 (0.00%)	1 / 200 (0.50%)	0 / 91 (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
Immune system disorders			
Anaphylactic shock			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypersensitivity			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaphylactic reaction			
subjects affected / exposed	0 / 206 (0.00%)	0 / 200 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Prostatitis			
subjects affected / exposed	0 / 206 (0.00%)	1 / 200 (0.50%)	0 / 91 (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			
Pleural effusion			

subjects affected / exposed	3 / 206 (1.46%)	0 / 200 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	2 / 206 (0.97%)	0 / 200 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	2 / 206 (0.97%)	0 / 200 (0.00%)	2 / 91 (2.20%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chylothorax			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (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
Oropharyngeal pain			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (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	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (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
Pneumonitis			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary arterial hypertension			

subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (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 failure			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	2 / 91 (2.20%)
occurrences causally related to treatment / all	0 / 1	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 206 (0.00%)	0 / 200 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	0 / 206 (0.00%)	0 / 200 (0.00%)	0 / 91 (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
Atelectasis			
subjects affected / exposed	0 / 206 (0.00%)	0 / 200 (0.00%)	0 / 91 (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
Hypoxia			
subjects affected / exposed	0 / 206 (0.00%)	0 / 200 (0.00%)	2 / 91 (2.20%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Pneumothorax spontaneous			
subjects affected / exposed	0 / 206 (0.00%)	1 / 200 (0.50%)	0 / 91 (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 oedema			
subjects affected / exposed	0 / 206 (0.00%)	1 / 200 (0.50%)	0 / 91 (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
Psychiatric disorders			
Agitation			

subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alcoholism			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (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
Binge drinking			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (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
Anxiety			
subjects affected / exposed	0 / 206 (0.00%)	0 / 200 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood creatinine increased			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (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
Liver function test abnormal			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (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
Neutrophil count decreased			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transaminases increased			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium test positive			

subjects affected / exposed	0 / 206 (0.00%)	1 / 200 (0.50%)	0 / 91 (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
International normalised ratio increased			
subjects affected / exposed	0 / 206 (0.00%)	0 / 200 (0.00%)	0 / 91 (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
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	3 / 206 (1.46%)	1 / 200 (0.50%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infusion related reaction			
subjects affected / exposed	3 / 206 (1.46%)	2 / 200 (1.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	3 / 3	2 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	2 / 206 (0.97%)	0 / 200 (0.00%)	0 / 91 (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
Head injury			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (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
Hip fracture			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (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
Humerus fracture			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint dislocation			

subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (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
Spinal fracture			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (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
Overdose			
subjects affected / exposed	0 / 206 (0.00%)	1 / 200 (0.50%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	1 / 1	1 / 1	1 / 1
Spinal compression fracture			
subjects affected / exposed	0 / 206 (0.00%)	0 / 200 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			
subjects affected / exposed	0 / 206 (0.00%)	0 / 200 (0.00%)	0 / 91 (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
Transfusion reaction			
subjects affected / exposed	0 / 206 (0.00%)	0 / 200 (0.00%)	0 / 91 (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
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	3 / 206 (1.46%)	0 / 200 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	3 / 206 (1.46%)	0 / 200 (0.00%)	2 / 91 (2.20%)
occurrences causally related to treatment / all	0 / 3	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			

subjects affected / exposed	2 / 206 (0.97%)	1 / 200 (0.50%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (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
Coronary artery disease			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial ischaemia			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (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
Acute coronary syndrome			
subjects affected / exposed	0 / 206 (0.00%)	0 / 200 (0.00%)	0 / 91 (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
Angina pectoris			
subjects affected / exposed	0 / 206 (0.00%)	0 / 200 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular block			

subjects affected / exposed	0 / 206 (0.00%)	1 / 200 (0.50%)	0 / 91 (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
Bradycardia			
subjects affected / exposed	0 / 206 (0.00%)	1 / 200 (0.50%)	0 / 91 (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
Cardiac failure congestive			
subjects affected / exposed	0 / 206 (0.00%)	0 / 200 (0.00%)	2 / 91 (2.20%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Left ventricular failure			
subjects affected / exposed	0 / 206 (0.00%)	0 / 200 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	0 / 206 (0.00%)	0 / 200 (0.00%)	0 / 91 (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
Pericarditis			
subjects affected / exposed	0 / 206 (0.00%)	0 / 200 (0.00%)	0 / 91 (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
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	3 / 206 (1.46%)	1 / 200 (0.50%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	2 / 206 (0.97%)	0 / 200 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cognitive disorder			

subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disturbance in attention			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalopathy			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (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
Haemorrhage intracranial			
subjects affected / exposed	1 / 206 (0.49%)	1 / 200 (0.50%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Headache			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Loss of consciousness			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (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	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (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
Brain oedema			
subjects affected / exposed	0 / 206 (0.00%)	0 / 200 (0.00%)	0 / 91 (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
Facial paresis			

subjects affected / exposed	0 / 206 (0.00%)	1 / 200 (0.50%)	0 / 91 (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
Intracranial mass			
subjects affected / exposed	0 / 206 (0.00%)	0 / 200 (0.00%)	0 / 91 (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
Neuralgia			
subjects affected / exposed	0 / 206 (0.00%)	1 / 200 (0.50%)	0 / 91 (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 aphasia			
subjects affected / exposed	0 / 206 (0.00%)	0 / 200 (0.00%)	0 / 91 (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
Transient ischaemic attack			
subjects affected / exposed	0 / 206 (0.00%)	0 / 200 (0.00%)	1 / 91 (1.10%)
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	2 / 206 (0.97%)	2 / 200 (1.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	1 / 2	2 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	3 / 206 (1.46%)	2 / 200 (1.00%)	2 / 91 (2.20%)
occurrences causally related to treatment / all	3 / 3	2 / 2	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemolysis			
subjects affected / exposed	0 / 206 (0.00%)	0 / 200 (0.00%)	0 / 91 (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
Neutropenia			

subjects affected / exposed	1 / 206 (0.49%)	3 / 200 (1.50%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	1 / 1	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (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
Thrombocytopenia			
subjects affected / exposed	0 / 206 (0.00%)	2 / 200 (1.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	2 / 3	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 206 (0.00%)	1 / 200 (0.50%)	0 / 91 (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
Eye disorders			
Exfoliation glaucoma			
subjects affected / exposed	0 / 206 (0.00%)	0 / 200 (0.00%)	0 / 91 (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
Eye inflammation			
subjects affected / exposed	0 / 206 (0.00%)	0 / 200 (0.00%)	0 / 91 (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
Glaucoma			
subjects affected / exposed	0 / 206 (0.00%)	0 / 200 (0.00%)	0 / 91 (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
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	3 / 206 (1.46%)	0 / 200 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	3 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Abdominal pain upper			
subjects affected / exposed	2 / 206 (0.97%)	0 / 200 (0.00%)	0 / 91 (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
Colitis			
subjects affected / exposed	2 / 206 (0.97%)	0 / 200 (0.00%)	0 / 91 (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
Abdominal pain			
subjects affected / exposed	1 / 206 (0.49%)	1 / 200 (0.50%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal fistula			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal stenosis			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (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
Enteritis			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (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	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric haemorrhage			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (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	1 / 206 (0.49%)	1 / 200 (0.50%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retroperitoneal haematoma			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (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
Retroperitoneal haemorrhage			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (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
Stomatitis			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer			
subjects affected / exposed	0 / 206 (0.00%)	0 / 200 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenogastric reflux			
subjects affected / exposed	0 / 206 (0.00%)	0 / 200 (0.00%)	0 / 91 (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
Haemorrhoids			
subjects affected / exposed	0 / 206 (0.00%)	1 / 200 (0.50%)	0 / 91 (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
Incarcerated inguinal hernia			
subjects affected / exposed	0 / 206 (0.00%)	0 / 200 (0.00%)	0 / 91 (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
Small intestinal haemorrhage			

subjects affected / exposed	0 / 206 (0.00%)	0 / 200 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 206 (0.00%)	0 / 200 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 206 (0.00%)	1 / 200 (0.50%)	0 / 91 (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
Hepatobiliary disorders			
Chronic hepatitis			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (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-induced liver injury			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholangitis			
subjects affected / exposed	0 / 206 (0.00%)	0 / 200 (0.00%)	0 / 91 (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
Cholecystitis			
subjects affected / exposed	0 / 206 (0.00%)	2 / 200 (1.00%)	0 / 91 (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
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	2 / 206 (0.97%)	0 / 200 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Drug eruption			

subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash maculo-papular			
subjects affected / exposed	0 / 206 (0.00%)	0 / 200 (0.00%)	0 / 91 (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
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 206 (0.00%)	0 / 200 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			
subjects affected / exposed	0 / 206 (0.00%)	1 / 200 (0.50%)	0 / 91 (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	0 / 206 (0.00%)	1 / 200 (0.50%)	0 / 91 (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
Endocrine disorders			
Adrenal mass			
subjects affected / exposed	0 / 206 (0.00%)	0 / 200 (0.00%)	1 / 91 (1.10%)
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			
Back pain			
subjects affected / exposed	2 / 206 (0.97%)	0 / 200 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Arthritis			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (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
Myalgia			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (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
Arthralgia			
subjects affected / exposed	0 / 206 (0.00%)	1 / 200 (0.50%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	21 / 206 (10.19%)	4 / 200 (2.00%)	4 / 91 (4.40%)
occurrences causally related to treatment / all	9 / 27	2 / 5	2 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	13 / 206 (6.31%)	0 / 200 (0.00%)	4 / 91 (4.40%)
occurrences causally related to treatment / all	2 / 15	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	10 / 206 (4.85%)	0 / 200 (0.00%)	8 / 91 (8.79%)
occurrences causally related to treatment / all	0 / 15	0 / 0	3 / 10
deaths causally related to treatment / all	0 / 0	0 / 0	2 / 2
Sepsis			

subjects affected / exposed	7 / 206 (3.40%)	1 / 200 (0.50%)	4 / 91 (4.40%)
occurrences causally related to treatment / all	4 / 7	1 / 1	0 / 4
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	5 / 206 (2.43%)	1 / 200 (0.50%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	3 / 5	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	4 / 206 (1.94%)	3 / 200 (1.50%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	1 / 4	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	2 / 206 (0.97%)	0 / 200 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	2 / 206 (0.97%)	0 / 200 (0.00%)	0 / 91 (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
Influenza			
subjects affected / exposed	2 / 206 (0.97%)	1 / 200 (0.50%)	0 / 91 (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
Klebsiella infection			
subjects affected / exposed	2 / 206 (0.97%)	0 / 200 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenic sepsis			
subjects affected / exposed	2 / 206 (0.97%)	0 / 200 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Pneumonia bacterial			

subjects affected / exposed	2 / 206 (0.97%)	0 / 200 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess limb			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (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
Bordetella infection			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopulmonary aspergillosis			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (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
Candida infection			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile infection			
subjects affected / exposed	1 / 206 (0.49%)	1 / 200 (0.50%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus infection			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytomegalovirus infection reactivation			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dientamoeba infection			

subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (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
Enterovirus infection			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (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
Medical device site joint infection			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orchitis			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (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
Osteomyelitis			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media acute			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parotitis			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (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
Peritonitis			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (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 streptococcal			

subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Progressive multifocal leukoencephalopathy			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Scrotal infection			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (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
Septic shock			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (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
Sinusitis			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (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
Bacteraemia			
subjects affected / exposed	0 / 206 (0.00%)	1 / 200 (0.50%)	0 / 91 (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
Clostridium difficile colitis			
subjects affected / exposed	0 / 206 (0.00%)	1 / 200 (0.50%)	0 / 91 (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
Cytomegalovirus colitis			
subjects affected / exposed	0 / 206 (0.00%)	0 / 200 (0.00%)	0 / 91 (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
Erysipelas			

subjects affected / exposed	0 / 206 (0.00%)	0 / 200 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Genitourinary tract infection			
subjects affected / exposed	0 / 206 (0.00%)	1 / 200 (0.50%)	0 / 91 (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
Infection			
subjects affected / exposed	0 / 206 (0.00%)	0 / 200 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver abscess			
subjects affected / exposed	0 / 206 (0.00%)	0 / 200 (0.00%)	0 / 91 (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
Meningitis bacterial			
subjects affected / exposed	0 / 206 (0.00%)	1 / 200 (0.50%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 206 (0.00%)	1 / 200 (0.50%)	0 / 91 (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
Pneumonia viral			
subjects affected / exposed	0 / 206 (0.00%)	0 / 200 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 206 (0.00%)	1 / 200 (0.50%)	0 / 91 (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
Metabolism and nutrition disorders			
Tumour lysis syndrome			

subjects affected / exposed	3 / 206 (1.46%)	3 / 200 (1.50%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	3 / 3	3 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	2 / 206 (0.97%)	0 / 200 (0.00%)	0 / 91 (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	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	1 / 91 (1.10%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	1 / 206 (0.49%)	0 / 200 (0.00%)	0 / 91 (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
Failure to thrive			
subjects affected / exposed	0 / 206 (0.00%)	0 / 200 (0.00%)	0 / 91 (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
Hyponatraemia			
subjects affected / exposed	0 / 206 (0.00%)	1 / 200 (0.50%)	0 / 91 (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

Serious adverse events	Arm D: Umbralisib		
Total subjects affected by serious adverse events			
subjects affected / exposed	34 / 86 (39.53%)		
number of deaths (all causes)	29		
number of deaths resulting from adverse events	1		

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Malignant melanoma			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Squamous cell carcinoma			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Adenocarcinoma			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Astrocytoma			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bladder transitional cell carcinoma			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Glioblastoma			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Lung adenocarcinoma				
subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neoplasm malignant				
subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Prostate cancer				
subjects affected / exposed	2 / 86 (2.33%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Squamous cell carcinoma of head and neck				
subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Squamous cell carcinoma of lung				
subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Adenocarcinoma pancreas				
subjects affected / exposed	1 / 86 (1.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Brain neoplasm				
subjects affected / exposed	1 / 86 (1.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Clear cell renal cell carcinoma				
subjects affected / exposed	0 / 86 (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 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metastases to central nervous system			
subjects affected / exposed	1 / 86 (1.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neuroendocrine carcinoma of the skin			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Plasma cell myeloma			
subjects affected / exposed	1 / 86 (1.16%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Aortic aneurysm			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Peripheral vascular disorder			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypertensive crisis			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Orthostatic hypotension			
subjects affected / exposed	1 / 86 (1.16%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular compression			

subjects affected / exposed	1 / 86 (1.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Death			
subjects affected / exposed	1 / 86 (1.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Oedema peripheral			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sudden cardiac death			
subjects affected / exposed	0 / 86 (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 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Adverse drug reaction			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Asthenia			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Mucosal inflammation			

subjects affected / exposed	1 / 86 (1.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sudden death			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Anaphylactic shock			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypersensitivity			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Anaphylactic reaction			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Prostatitis			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			

subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				
subjects affected / exposed	1 / 86 (1.16%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	1 / 86 (1.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Chronic obstructive pulmonary disease				
subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chylothorax				
subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oropharyngeal pain				
subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia aspiration				
subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonitis				
subjects affected / exposed	1 / 86 (1.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary arterial hypertension				

subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory failure			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Acute respiratory failure			
subjects affected / exposed	1 / 86 (1.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Atelectasis			
subjects affected / exposed	1 / 86 (1.16%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hypoxia			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumothorax spontaneous			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulmonary oedema			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Agitation			

subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Alcoholism			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Binge drinking			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Anxiety			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
Blood creatinine increased			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Liver function test abnormal			
subjects affected / exposed	0 / 86 (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 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Transaminases increased			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Clostridium test positive			

subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
International normalised ratio increased			
subjects affected / exposed	1 / 86 (1.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infusion related reaction			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fall			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Head injury			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hip fracture			
subjects affected / exposed	1 / 86 (1.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Humerus fracture			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Joint dislocation			

subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Spinal fracture			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Overdose			
subjects affected / exposed	1 / 86 (1.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	1 / 1		
Spinal compression fracture			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tibia fracture			
subjects affected / exposed	1 / 86 (1.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Transfusion reaction			
subjects affected / exposed	1 / 86 (1.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Atrial fibrillation			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Myocardial infarction			

subjects affected / exposed	1 / 86 (1.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Angina unstable				
subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac arrest				
subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure				
subjects affected / exposed	0 / 86 (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 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myocardial ischaemia				
subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute coronary syndrome				
subjects affected / exposed	1 / 86 (1.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Angina pectoris				
subjects affected / exposed	1 / 86 (1.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Atrioventricular block				

subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bradycardia			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac failure congestive			
subjects affected / exposed	1 / 86 (1.16%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Left ventricular failure			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pericardial effusion			
subjects affected / exposed	1 / 86 (1.16%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pericarditis			
subjects affected / exposed	1 / 86 (1.16%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 86 (1.16%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Dizziness			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cognitive disorder			

subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Disturbance in attention				
subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Encephalopathy				
subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemorrhage intracranial				
subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Headache				
subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Loss of consciousness				
subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Seizure				
subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Brain oedema				
subjects affected / exposed	1 / 86 (1.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Facial paresis				

subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intracranial mass			
subjects affected / exposed	1 / 86 (1.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neuralgia			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Transient aphasia			
subjects affected / exposed	1 / 86 (1.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Transient ischaemic attack			
subjects affected / exposed	0 / 86 (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	3 / 86 (3.49%)		
occurrences causally related to treatment / all	3 / 5		
deaths causally related to treatment / all	0 / 0		
Febrile neutropenia			
subjects affected / exposed	2 / 86 (2.33%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Haemolysis			
subjects affected / exposed	1 / 86 (1.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neutropenia			

subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pancytopenia			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Exfoliation glaucoma			
subjects affected / exposed	1 / 86 (1.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye inflammation			
subjects affected / exposed	1 / 86 (1.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Glaucoma			
subjects affected / exposed	1 / 86 (1.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Abdominal pain upper				
subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Colitis				
subjects affected / exposed	1 / 86 (1.16%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Abdominal pain				
subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Anal fistula				
subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Anal stenosis				
subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Enteritis				
subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Enterocolitis				
subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastric haemorrhage				
subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nausea				

subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Retroperitoneal haematoma				
subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Retroperitoneal haemorrhage				
subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Stomatitis				
subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Duodenal ulcer				
subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Duodenogastric reflux				
subjects affected / exposed	1 / 86 (1.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Haemorrhoids				
subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Incarcerated inguinal hernia				
subjects affected / exposed	1 / 86 (1.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Small intestinal haemorrhage				

subjects affected / exposed	0 / 86 (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 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	1 / 86 (1.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Chronic hepatitis			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Drug-induced liver injury			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cholangitis			
subjects affected / exposed	1 / 86 (1.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cholecystitis			
subjects affected / exposed	1 / 86 (1.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Drug eruption			

subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rash			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rash maculo-papular			
subjects affected / exposed	1 / 86 (1.16%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 86 (1.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haematuria			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal failure			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Adrenal mass			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Arthritis			
subjects affected / exposed	1 / 86 (1.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Muscular weakness			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Myalgia			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Osteoarthritis			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Arthralgia			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
COVID-19			
subjects affected / exposed	1 / 86 (1.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
COVID-19 pneumonia			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sepsis			

subjects affected / exposed	2 / 86 (2.33%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
subjects affected / exposed	1 / 86 (1.16%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Bronchitis				
subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Influenza				
subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Klebsiella infection				
subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neutropenic sepsis				
subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia bacterial				

subjects affected / exposed	1 / 86 (1.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Abscess limb				
subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bordetella infection				
subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchopulmonary aspergillosis				
subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Candida infection				
subjects affected / exposed	0 / 86 (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 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cytomegalovirus infection				
subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cytomegalovirus infection reactivation				
subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dientamoeba infection				

subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Enterovirus infection				
subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Medical device site joint infection				
subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Orchitis				
subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osteomyelitis				
subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Otitis media acute				
subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Parotitis				
subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peritonitis				
subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia streptococcal				

subjects affected / exposed	0 / 86 (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 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Scrotal infection				
subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Septic shock				
subjects affected / exposed	1 / 86 (1.16%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sinusitis				
subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bacteraemia				
subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Clostridium difficile colitis				
subjects affected / exposed	0 / 86 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cytomegalovirus colitis				
subjects affected / exposed	1 / 86 (1.16%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Erysipelas				

subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Genitourinary tract infection			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infection			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Liver abscess			
subjects affected / exposed	1 / 86 (1.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Meningitis bacterial			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia viral			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Tumour lysis syndrome			

subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypoglycaemia			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dehydration			
subjects affected / exposed	1 / 86 (1.16%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hyperkalaemia			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypokalaemia			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Failure to thrive			
subjects affected / exposed	1 / 86 (1.16%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	0 / 86 (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	Arm A: Ublituximab + Umbralisib	Arm B: Obinutuzumab + Chlorambucil	Arm C: Ublituximab
Total subjects affected by non-serious adverse events			
subjects affected / exposed	205 / 206 (99.51%)	189 / 200 (94.50%)	84 / 91 (92.31%)
Vascular disorders			
Hypertension			
subjects affected / exposed	27 / 206 (13.11%)	8 / 200 (4.00%)	9 / 91 (9.89%)
occurrences (all)	42	15	22
Flushing			
subjects affected / exposed	16 / 206 (7.77%)	18 / 200 (9.00%)	9 / 91 (9.89%)
occurrences (all)	19	20	12
Hypotension			
subjects affected / exposed	13 / 206 (6.31%)	17 / 200 (8.50%)	12 / 91 (13.19%)
occurrences (all)	13	19	14
Hot flush			
subjects affected / exposed	9 / 206 (4.37%)	10 / 200 (5.00%)	4 / 91 (4.40%)
occurrences (all)	9	10	4
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	76 / 206 (36.89%)	60 / 200 (30.00%)	28 / 91 (30.77%)
occurrences (all)	158	81	39
Pyrexia			
subjects affected / exposed	53 / 206 (25.73%)	38 / 200 (19.00%)	22 / 91 (24.18%)
occurrences (all)	88	49	27
Chills			
subjects affected / exposed	52 / 206 (25.24%)	33 / 200 (16.50%)	25 / 91 (27.47%)
occurrences (all)	64	43	29
Oedema peripheral			
subjects affected / exposed	39 / 206 (18.93%)	12 / 200 (6.00%)	10 / 91 (10.99%)
occurrences (all)	49	14	14
Asthenia			
subjects affected / exposed	25 / 206 (12.14%)	13 / 200 (6.50%)	4 / 91 (4.40%)
occurrences (all)	31	16	5
Pain			
subjects affected / exposed	13 / 206 (6.31%)	4 / 200 (2.00%)	3 / 91 (3.30%)
occurrences (all)	20	6	4
Chest discomfort			

subjects affected / exposed occurrences (all)	12 / 206 (5.83%) 12	7 / 200 (3.50%) 7	3 / 91 (3.30%) 4
Influenza like illness subjects affected / exposed occurrences (all)	12 / 206 (5.83%) 18	9 / 200 (4.50%) 9	2 / 91 (2.20%) 2
Non-cardiac chest pain subjects affected / exposed occurrences (all)	4 / 206 (1.94%) 5	6 / 200 (3.00%) 7	6 / 91 (6.59%) 6
Immune system disorders Hypogammaglobulinaemia subjects affected / exposed occurrences (all)	19 / 206 (9.22%) 20	5 / 200 (2.50%) 7	2 / 91 (2.20%) 2
Seasonal allergy subjects affected / exposed occurrences (all)	3 / 206 (1.46%) 3	2 / 200 (1.00%) 2	6 / 91 (6.59%) 7
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	62 / 206 (30.10%) 105	36 / 200 (18.00%) 42	18 / 91 (19.78%) 31
Dyspnoea subjects affected / exposed occurrences (all)	41 / 206 (19.90%) 51	34 / 200 (17.00%) 35	20 / 91 (21.98%) 29
Productive cough subjects affected / exposed occurrences (all)	14 / 206 (6.80%) 21	3 / 200 (1.50%) 3	5 / 91 (5.49%) 6
Nasal congestion subjects affected / exposed occurrences (all)	10 / 206 (4.85%) 13	2 / 200 (1.00%) 2	7 / 91 (7.69%) 8
Epistaxis subjects affected / exposed occurrences (all)	7 / 206 (3.40%) 8	10 / 200 (5.00%) 12	2 / 91 (2.20%) 2
Dyspnoea exertional subjects affected / exposed occurrences (all)	6 / 206 (2.91%) 7	3 / 200 (1.50%) 3	6 / 91 (6.59%) 7
Psychiatric disorders			

Insomnia			
subjects affected / exposed	41 / 206 (19.90%)	28 / 200 (14.00%)	12 / 91 (13.19%)
occurrences (all)	51	33	14
Anxiety			
subjects affected / exposed	24 / 206 (11.65%)	11 / 200 (5.50%)	4 / 91 (4.40%)
occurrences (all)	35	13	4
Depression			
subjects affected / exposed	11 / 206 (5.34%)	6 / 200 (3.00%)	4 / 91 (4.40%)
occurrences (all)	12	7	5
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	34 / 206 (16.50%)	9 / 200 (4.50%)	6 / 91 (6.59%)
occurrences (all)	62	17	6
Aspartate aminotransferase increased			
subjects affected / exposed	29 / 206 (14.08%)	9 / 200 (4.50%)	6 / 91 (6.59%)
occurrences (all)	50	11	9
Neutrophil count decreased			
subjects affected / exposed	28 / 206 (13.59%)	21 / 200 (10.50%)	6 / 91 (6.59%)
occurrences (all)	74	53	12
Platelet count decreased			
subjects affected / exposed	21 / 206 (10.19%)	19 / 200 (9.50%)	10 / 91 (10.99%)
occurrences (all)	39	75	14
Weight decreased			
subjects affected / exposed	16 / 206 (7.77%)	4 / 200 (2.00%)	4 / 91 (4.40%)
occurrences (all)	18	4	6
Blood creatinine increased			
subjects affected / exposed	14 / 206 (6.80%)	10 / 200 (5.00%)	6 / 91 (6.59%)
occurrences (all)	25	10	7
White blood cell count decreased			
subjects affected / exposed	10 / 206 (4.85%)	17 / 200 (8.50%)	8 / 91 (8.79%)
occurrences (all)	21	33	19
Blood lactate dehydrogenase increased			
subjects affected / exposed	5 / 206 (2.43%)	0 / 200 (0.00%)	5 / 91 (5.49%)
occurrences (all)	6	0	5
Lymphocyte count increased			

subjects affected / exposed occurrences (all)	3 / 206 (1.46%) 3	2 / 200 (1.00%) 2	0 / 91 (0.00%) 0
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	92 / 206 (44.66%)	49 / 200 (24.50%)	36 / 91 (39.56%)
occurrences (all)	115	58	72
Contusion			
subjects affected / exposed	18 / 206 (8.74%)	9 / 200 (4.50%)	7 / 91 (7.69%)
occurrences (all)	19	15	7
Fall			
subjects affected / exposed	13 / 206 (6.31%)	4 / 200 (2.00%)	6 / 91 (6.59%)
occurrences (all)	17	4	9
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	6 / 206 (2.91%)	3 / 200 (1.50%)	5 / 91 (5.49%)
occurrences (all)	6	3	9
Nervous system disorders			
Headache			
subjects affected / exposed	56 / 206 (27.18%)	36 / 200 (18.00%)	18 / 91 (19.78%)
occurrences (all)	80	52	27
Dizziness			
subjects affected / exposed	46 / 206 (22.33%)	19 / 200 (9.50%)	14 / 91 (15.38%)
occurrences (all)	92	21	19
Dysgeusia			
subjects affected / exposed	26 / 206 (12.62%)	3 / 200 (1.50%)	1 / 91 (1.10%)
occurrences (all)	59	3	1
Tremor			
subjects affected / exposed	13 / 206 (6.31%)	3 / 200 (1.50%)	5 / 91 (5.49%)
occurrences (all)	17	4	7
Paraesthesia			
subjects affected / exposed	9 / 206 (4.37%)	5 / 200 (2.50%)	1 / 91 (1.10%)
occurrences (all)	13	6	1
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	70 / 206 (33.98%)	79 / 200 (39.50%)	25 / 91 (27.47%)
occurrences (all)	210	165	41

Anaemia			
subjects affected / exposed	29 / 206 (14.08%)	25 / 200 (12.50%)	15 / 91 (16.48%)
occurrences (all)	59	52	24
Thrombocytopenia			
subjects affected / exposed	21 / 206 (10.19%)	44 / 200 (22.00%)	13 / 91 (14.29%)
occurrences (all)	44	90	20
Eye disorders			
Vision blurred			
subjects affected / exposed	14 / 206 (6.80%)	6 / 200 (3.00%)	4 / 91 (4.40%)
occurrences (all)	17	6	4
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	118 / 206 (57.28%)	45 / 200 (22.50%)	24 / 91 (26.37%)
occurrences (all)	295	66	30
Nausea			
subjects affected / exposed	105 / 206 (50.97%)	75 / 200 (37.50%)	27 / 91 (29.67%)
occurrences (all)	179	109	38
Constipation			
subjects affected / exposed	38 / 206 (18.45%)	23 / 200 (11.50%)	14 / 91 (15.38%)
occurrences (all)	41	24	18
Vomiting			
subjects affected / exposed	38 / 206 (18.45%)	29 / 200 (14.50%)	9 / 91 (9.89%)
occurrences (all)	58	31	14
Abdominal pain			
subjects affected / exposed	27 / 206 (13.11%)	19 / 200 (9.50%)	9 / 91 (9.89%)
occurrences (all)	59	24	9
Dyspepsia			
subjects affected / exposed	24 / 206 (11.65%)	9 / 200 (4.50%)	3 / 91 (3.30%)
occurrences (all)	46	10	3
Abdominal pain upper			
subjects affected / exposed	15 / 206 (7.28%)	5 / 200 (2.50%)	1 / 91 (1.10%)
occurrences (all)	18	6	2
Abdominal distension			
subjects affected / exposed	13 / 206 (6.31%)	2 / 200 (1.00%)	5 / 91 (5.49%)
occurrences (all)	16	2	5
Gastrooesophageal reflux disease			

subjects affected / exposed	12 / 206 (5.83%)	5 / 200 (2.50%)	6 / 91 (6.59%)
occurrences (all)	14	5	7
Stomatitis			
subjects affected / exposed	12 / 206 (5.83%)	2 / 200 (1.00%)	0 / 91 (0.00%)
occurrences (all)	20	2	0
Flatulence			
subjects affected / exposed	9 / 206 (4.37%)	3 / 200 (1.50%)	0 / 91 (0.00%)
occurrences (all)	12	3	0
Colitis			
subjects affected / exposed	7 / 206 (3.40%)	0 / 200 (0.00%)	1 / 91 (1.10%)
occurrences (all)	8	0	1
Gastritis			
subjects affected / exposed	7 / 206 (3.40%)	0 / 200 (0.00%)	0 / 91 (0.00%)
occurrences (all)	8	0	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	17 / 206 (8.25%)	3 / 200 (1.50%)	8 / 91 (8.79%)
occurrences (all)	22	3	9
Night sweats			
subjects affected / exposed	12 / 206 (5.83%)	6 / 200 (3.00%)	9 / 91 (9.89%)
occurrences (all)	16	6	13
Dry skin			
subjects affected / exposed	11 / 206 (5.34%)	2 / 200 (1.00%)	1 / 91 (1.10%)
occurrences (all)	12	2	1
Rash maculo-papular			
subjects affected / exposed	10 / 206 (4.85%)	5 / 200 (2.50%)	1 / 91 (1.10%)
occurrences (all)	14	5	1
Pruritus			
subjects affected / exposed	9 / 206 (4.37%)	6 / 200 (3.00%)	3 / 91 (3.30%)
occurrences (all)	10	8	6
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	14 / 206 (6.80%)	5 / 200 (2.50%)	1 / 91 (1.10%)
occurrences (all)	23	5	1
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	32 / 206 (15.53%)	16 / 200 (8.00%)	16 / 91 (17.58%)
occurrences (all)	47	21	29
Back pain			
subjects affected / exposed	32 / 206 (15.53%)	15 / 200 (7.50%)	12 / 91 (13.19%)
occurrences (all)	46	18	13
Myalgia			
subjects affected / exposed	20 / 206 (9.71%)	11 / 200 (5.50%)	4 / 91 (4.40%)
occurrences (all)	32	11	4
Pain in extremity			
subjects affected / exposed	20 / 206 (9.71%)	15 / 200 (7.50%)	10 / 91 (10.99%)
occurrences (all)	26	19	13
Muscle spasms			
subjects affected / exposed	11 / 206 (5.34%)	7 / 200 (3.50%)	8 / 91 (8.79%)
occurrences (all)	11	7	8
Musculoskeletal chest pain			
subjects affected / exposed	11 / 206 (5.34%)	3 / 200 (1.50%)	1 / 91 (1.10%)
occurrences (all)	13	3	1
Neck pain			
subjects affected / exposed	6 / 206 (2.91%)	3 / 200 (1.50%)	5 / 91 (5.49%)
occurrences (all)	7	4	6
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	48 / 206 (23.30%)	26 / 200 (13.00%)	16 / 91 (17.58%)
occurrences (all)	84	29	22
Pneumonia			
subjects affected / exposed	27 / 206 (13.11%)	11 / 200 (5.50%)	10 / 91 (10.99%)
occurrences (all)	36	11	12
Urinary tract infection			
subjects affected / exposed	26 / 206 (12.62%)	4 / 200 (2.00%)	10 / 91 (10.99%)
occurrences (all)	42	6	18
Sinusitis			
subjects affected / exposed	25 / 206 (12.14%)	7 / 200 (3.50%)	6 / 91 (6.59%)
occurrences (all)	35	7	9
Bronchitis			

subjects affected / exposed occurrences (all)	20 / 206 (9.71%) 24	5 / 200 (2.50%) 5	5 / 91 (5.49%) 7
COVID-19 subjects affected / exposed occurrences (all)	17 / 206 (8.25%) 22	0 / 200 (0.00%) 0	6 / 91 (6.59%) 6
Clostridium difficile infection subjects affected / exposed occurrences (all)	2 / 206 (0.97%) 2	1 / 200 (0.50%) 1	0 / 91 (0.00%) 0
Herpes zoster subjects affected / exposed occurrences (all)	1 / 206 (0.49%) 1	1 / 200 (0.50%) 1	7 / 91 (7.69%) 7
Metabolism and nutrition disorders			
Decreased appetite subjects affected / exposed occurrences (all)	42 / 206 (20.39%) 49	18 / 200 (9.00%) 19	6 / 91 (6.59%) 10
Hypokalaemia subjects affected / exposed occurrences (all)	29 / 206 (14.08%) 37	4 / 200 (2.00%) 5	2 / 91 (2.20%) 2
Hypomagnesaemia subjects affected / exposed occurrences (all)	15 / 206 (7.28%) 19	6 / 200 (3.00%) 6	3 / 91 (3.30%) 3
Hypocalcaemia subjects affected / exposed occurrences (all)	13 / 206 (6.31%) 23	5 / 200 (2.50%) 6	5 / 91 (5.49%) 5
Hypophosphataemia subjects affected / exposed occurrences (all)	13 / 206 (6.31%) 37	1 / 200 (0.50%) 1	4 / 91 (4.40%) 5
Dehydration subjects affected / exposed occurrences (all)	12 / 206 (5.83%) 20	7 / 200 (3.50%) 10	3 / 91 (3.30%) 3
Hyperuricaemia subjects affected / exposed occurrences (all)	10 / 206 (4.85%) 14	5 / 200 (2.50%) 5	5 / 91 (5.49%) 5
Hyperglycaemia subjects affected / exposed occurrences (all)	8 / 206 (3.88%) 15	6 / 200 (3.00%) 11	5 / 91 (5.49%) 7

Non-serious adverse events	Arm D: Umbralisib		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	84 / 86 (97.67%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	16 / 86 (18.60%)		
occurrences (all)	31		
Flushing			
subjects affected / exposed	2 / 86 (2.33%)		
occurrences (all)	2		
Hypotension			
subjects affected / exposed	3 / 86 (3.49%)		
occurrences (all)	4		
Hot flush			
subjects affected / exposed	4 / 86 (4.65%)		
occurrences (all)	6		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	22 / 86 (25.58%)		
occurrences (all)	32		
Pyrexia			
subjects affected / exposed	11 / 86 (12.79%)		
occurrences (all)	13		
Chills			
subjects affected / exposed	12 / 86 (13.95%)		
occurrences (all)	15		
Oedema peripheral			
subjects affected / exposed	9 / 86 (10.47%)		
occurrences (all)	15		
Asthenia			
subjects affected / exposed	4 / 86 (4.65%)		
occurrences (all)	4		
Pain			
subjects affected / exposed	1 / 86 (1.16%)		
occurrences (all)	1		
Chest discomfort			

subjects affected / exposed occurrences (all)	0 / 86 (0.00%) 0		
Influenza like illness subjects affected / exposed occurrences (all)	2 / 86 (2.33%) 2		
Non-cardiac chest pain subjects affected / exposed occurrences (all)	2 / 86 (2.33%) 2		
Immune system disorders Hypogammaglobulinaemia subjects affected / exposed occurrences (all)	0 / 86 (0.00%) 0		
Seasonal allergy subjects affected / exposed occurrences (all)	2 / 86 (2.33%) 2		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	18 / 86 (20.93%) 29		
Dyspnoea subjects affected / exposed occurrences (all)	14 / 86 (16.28%) 22		
Productive cough subjects affected / exposed occurrences (all)	2 / 86 (2.33%) 2		
Nasal congestion subjects affected / exposed occurrences (all)	6 / 86 (6.98%) 7		
Epistaxis subjects affected / exposed occurrences (all)	1 / 86 (1.16%) 5		
Dyspnoea exertional subjects affected / exposed occurrences (all)	0 / 86 (0.00%) 0		
Psychiatric disorders			

Insomnia			
subjects affected / exposed	7 / 86 (8.14%)		
occurrences (all)	9		
Anxiety			
subjects affected / exposed	5 / 86 (5.81%)		
occurrences (all)	5		
Depression			
subjects affected / exposed	4 / 86 (4.65%)		
occurrences (all)	5		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	13 / 86 (15.12%)		
occurrences (all)	33		
Aspartate aminotransferase increased			
subjects affected / exposed	11 / 86 (12.79%)		
occurrences (all)	26		
Neutrophil count decreased			
subjects affected / exposed	6 / 86 (6.98%)		
occurrences (all)	15		
Platelet count decreased			
subjects affected / exposed	4 / 86 (4.65%)		
occurrences (all)	10		
Weight decreased			
subjects affected / exposed	10 / 86 (11.63%)		
occurrences (all)	10		
Blood creatinine increased			
subjects affected / exposed	7 / 86 (8.14%)		
occurrences (all)	8		
White blood cell count decreased			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences (all)	0		
Blood lactate dehydrogenase increased			
subjects affected / exposed	5 / 86 (5.81%)		
occurrences (all)	7		
Lymphocyte count increased			

subjects affected / exposed occurrences (all)	5 / 86 (5.81%) 7		
Injury, poisoning and procedural complications Infusion related reaction subjects affected / exposed occurrences (all) Contusion subjects affected / exposed occurrences (all) Fall subjects affected / exposed occurrences (all)	0 / 86 (0.00%) 0 8 / 86 (9.30%) 11 4 / 86 (4.65%) 4		
Cardiac disorders Atrial fibrillation subjects affected / exposed occurrences (all)	1 / 86 (1.16%) 1		
Nervous system disorders Headache subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all) Dysgeusia subjects affected / exposed occurrences (all) Tremor subjects affected / exposed occurrences (all) Paraesthesia subjects affected / exposed occurrences (all)	17 / 86 (19.77%) 23 17 / 86 (19.77%) 28 8 / 86 (9.30%) 12 1 / 86 (1.16%) 1 5 / 86 (5.81%) 7		
Blood and lymphatic system disorders Neutropenia subjects affected / exposed occurrences (all)	15 / 86 (17.44%) 31		

Anaemia			
subjects affected / exposed	18 / 86 (20.93%)		
occurrences (all)	32		
Thrombocytopenia			
subjects affected / exposed	7 / 86 (8.14%)		
occurrences (all)	10		
Eye disorders			
Vision blurred			
subjects affected / exposed	7 / 86 (8.14%)		
occurrences (all)	8		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	54 / 86 (62.79%)		
occurrences (all)	119		
Nausea			
subjects affected / exposed	34 / 86 (39.53%)		
occurrences (all)	66		
Constipation			
subjects affected / exposed	12 / 86 (13.95%)		
occurrences (all)	15		
Vomiting			
subjects affected / exposed	14 / 86 (16.28%)		
occurrences (all)	22		
Abdominal pain			
subjects affected / exposed	6 / 86 (6.98%)		
occurrences (all)	8		
Dyspepsia			
subjects affected / exposed	5 / 86 (5.81%)		
occurrences (all)	5		
Abdominal pain upper			
subjects affected / exposed	5 / 86 (5.81%)		
occurrences (all)	8		
Abdominal distension			
subjects affected / exposed	4 / 86 (4.65%)		
occurrences (all)	5		
Gastrooesophageal reflux disease			

subjects affected / exposed	1 / 86 (1.16%)		
occurrences (all)	1		
Stomatitis			
subjects affected / exposed	6 / 86 (6.98%)		
occurrences (all)	6		
Flatulence			
subjects affected / exposed	8 / 86 (9.30%)		
occurrences (all)	8		
Colitis			
subjects affected / exposed	6 / 86 (6.98%)		
occurrences (all)	8		
Gastritis			
subjects affected / exposed	5 / 86 (5.81%)		
occurrences (all)	5		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	10 / 86 (11.63%)		
occurrences (all)	16		
Night sweats			
subjects affected / exposed	6 / 86 (6.98%)		
occurrences (all)	7		
Dry skin			
subjects affected / exposed	5 / 86 (5.81%)		
occurrences (all)	5		
Rash maculo-papular			
subjects affected / exposed	5 / 86 (5.81%)		
occurrences (all)	7		
Pruritus			
subjects affected / exposed	8 / 86 (9.30%)		
occurrences (all)	17		
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	2 / 86 (2.33%)		
occurrences (all)	3		
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	18 / 86 (20.93%)		
occurrences (all)	28		
Back pain			
subjects affected / exposed	14 / 86 (16.28%)		
occurrences (all)	21		
Myalgia			
subjects affected / exposed	9 / 86 (10.47%)		
occurrences (all)	12		
Pain in extremity			
subjects affected / exposed	9 / 86 (10.47%)		
occurrences (all)	14		
Muscle spasms			
subjects affected / exposed	5 / 86 (5.81%)		
occurrences (all)	7		
Musculoskeletal chest pain			
subjects affected / exposed	2 / 86 (2.33%)		
occurrences (all)	2		
Neck pain			
subjects affected / exposed	2 / 86 (2.33%)		
occurrences (all)	3		
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	18 / 86 (20.93%)		
occurrences (all)	22		
Pneumonia			
subjects affected / exposed	6 / 86 (6.98%)		
occurrences (all)	6		
Urinary tract infection			
subjects affected / exposed	2 / 86 (2.33%)		
occurrences (all)	2		
Sinusitis			
subjects affected / exposed	2 / 86 (2.33%)		
occurrences (all)	2		
Bronchitis			

subjects affected / exposed	4 / 86 (4.65%)		
occurrences (all)	6		
COVID-19			
subjects affected / exposed	6 / 86 (6.98%)		
occurrences (all)	7		
Clostridium difficile infection			
subjects affected / exposed	5 / 86 (5.81%)		
occurrences (all)	5		
Herpes zoster			
subjects affected / exposed	2 / 86 (2.33%)		
occurrences (all)	2		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	14 / 86 (16.28%)		
occurrences (all)	22		
Hypokalaemia			
subjects affected / exposed	11 / 86 (12.79%)		
occurrences (all)	18		
Hypomagnesaemia			
subjects affected / exposed	2 / 86 (2.33%)		
occurrences (all)	2		
Hypocalcaemia			
subjects affected / exposed	0 / 86 (0.00%)		
occurrences (all)	0		
Hypophosphataemia			
subjects affected / exposed	3 / 86 (3.49%)		
occurrences (all)	6		
Dehydration			
subjects affected / exposed	5 / 86 (5.81%)		
occurrences (all)	5		
Hyperuricaemia			
subjects affected / exposed	3 / 86 (3.49%)		
occurrences (all)	4		
Hyperglycaemia			
subjects affected / exposed	5 / 86 (5.81%)		
occurrences (all)	19		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 June 2016	Version 2.0: Subjects randomized to Arms A and D are now required to start prophylaxis treatment with pneumocystis jiroveci pneumonia (PCP) and antiviral therapy within 7 days prior to randomization (Section 6.2.4), whereas this was previously at investigator discretion. The phrasing of response assessment intervals has been revised for clarity from "prior to cycles 4, 7, 10, and 13 at Weeks 12, 24, 36, 48, and every 3 cycles after," to "after the completion of cycles 3, 6, 9, 12, 15, 18 and every 3 cycles thereafter" and it was further clarified that subjects being followed for PFS off treatment should have evaluations done every 12 weeks. The shelf life of ublituximab has been increased to 36 months from 24 months when stored between +2 C / +8 C to reflect newly available stability data on ublituximab drug product.
10 April 2017	Version 3.0 : Language was inserted to support the planned interim analysis for contribution amongst the first 200 subjects and facilitate the discontinuation of Arms C and D should the interim analysis indicate these arms are to be discontinued. Overall Survival (OS) has been added to the efficacy endpoints. MRD will now be evaluated in all subjects achieving a PR or CR following the Cycle 6 response assessment as opposed to previously only in subjects achieving a CR. MRD sampling window was changed from a +/- 7 day window to +/- 14 day window. TGR-1202 dose delay/modification section was updated for non-hematologic toxicity specific for diarrhea. Ublituximab dose delay/modification section was updated for management of anaphylaxis.
18 June 2017	Version 3.1: Section 6.2.3.3.1 and Section 7.3 were both updated to include information regarding a new vial size for ublituximab. Inclusion criteria 1d – added the micro symbol "μ" as was left off in error.
04 October 2017	Version 4.0: Section 4 was updated to reflect the closing of Arms C and D pursuant to the pre-specified interim analysis to establish contribution, conducted by the Data Safety Monitoring Board (DSMB) in May 2017. Section 5.1.4 was updated to clarify that an additional post-baseline sparse PK sample could be collected from subjects. Updates were made throughout to include the generic name of TGR-1202: umbralisib and Minor administrative updates and typographical errors were corrected throughout.
20 December 2017	Version 4.1: Sections 6.3 and 7.3: Acknowledgement of the Adverse Event "Anaphylaxis" was mistakenly removed from Version 4.0 and has been re-inserted into the respected sections.

13 February 2019	Version 5.0: Updated response assessment guidelines to state: "During the study period, Response assessments should be obtained every 3 cycles for the first 24 cycles. After Cycle 24, evaluate for response approximately every 6 cycles unless clinically indicated sooner. Subjects followed for PFS off treatment should have response assessments done approximately every 6 months unless clinically indicated sooner. Section 5.1.1. cytomegalovirus (CMV) surveillance added for all subjects on Arms A and D every 3 months through 30 days from last dose of study drug (EOT Visit). Section 6.2.3 modified: Recommendations for antihypertensives prior to Ublituximab infusion. Window for holding antihypertensive is changed. Consider holding antihypertensives 12-24 hours prior to infusion from previously stated 24 hours. Premedication timing clarified. Section 6.2.4 was updated to remove Bactrim as a recommended pneumocystis jiroveci pneumonia (anti-PCP) prophylaxis, and additional instructions were given to switch to an alternate prophylaxis therapy, reduce dose, or discontinue prophylaxis at investigator discretion.
15 March 2020	Version 6.0: Response categories of CRi (complete response with incomplete marrow recovery) and nPR (nodular PR) were added throughout. Terminology of tumor status and tumor assessment were changed to disease assessment throughout. Updates to the statistical analysis plan were integrated throughout, including: a. The interim analysis for purposes of futility at 75% of target events was converted to an interim analysis of efficacy consistent with updates to the Statistical Analysis Plan (SAP); b. MRD negativity rate was modified to remove reference to "MRD positivity at baseline" since no baseline MRD samples are to be obtained in the study. MRD was clarified as being assessed amongst responders only. c. Clarification was made to specify that the primary and secondary efficacy analyses would occur in the ITT population. d. The timing of the ORR analysis was clarified to be following a positive interim PFS analysis or, if the interim PFS analysis is negative, following the final PFS analysis; Section 10.9.3 was updated to fix an error in the required reporting of deaths due to disease progression on study which should NOT be reported as an adverse event. Minor administrative and editorial changes were incorporated.

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 sponsor's business decision, the clinical trial was terminated by the sponsor prematurely. As such, the study results are reflective of the data captured to the time of study termination and with limited data verification.

Notes: