Clinical trial results:
A Phase 2 Study to Evaluate the Efficacy and Tolerability of Debio 1562 in Combination with Rituximab in Patients with Relapsed and/or Refractory Diffuse Large B-Cell Lymphoma and Other Forms of Non-Hodgkin's Lymphoma

Summary

EudraCT number	2015-004061-87
Trial protocol	BE HU BG CZ PL IT
Global end of trial date	25 June 2021

Results information

Result version number	v1
This version publication date	09 July 2022
First version publication date	09 July 2022

Trial information

Trial identification

Sponsor protocol code	Debio 1562-201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02564744
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Debiopharm International S.A.
Sponsor organisation address	Chemin Messidor 5-7, Lausanne, Switzerland, CH-1006
Public contact	Clinical Department, Debiopharm International S.A., +41 213210111, ClinicalTrials@debiopharm.com
Scientific contact	Clinical Department, Debiopharm International S.A., +41 213210111, ClinicalTrials@debiopharm.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	25 June 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	25 June 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the safety, tolerability, and anti-tumor activity of the proposed Debio 1562 dose regimens in combination with rituximab.

Protection of trial subjects:

Written approval of the study protocol and the informed consent was obtained from the independent ethics committee (IEC), prior to initiation of the study. The study was conducted in accordance with local regulations, Good Clinical Practice (GCP), International Council for Harmonisation (ICH) notes for GCP (ICH/CPMP/135/95), and ethical principles that have their origin in the Declaration of Helsinki and its amendments.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 June 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 7
Country: Number of subjects enrolled	Belgium: 14
Country: Number of subjects enrolled	Bulgaria: 7
Country: Number of subjects enrolled	Czechia: 10
Country: Number of subjects enrolled	Hungary: 8
Country: Number of subjects enrolled	Italy: 7
Country: Number of subjects enrolled	Switzerland: 1
Country: Number of subjects enrolled	Ukraine: 14
Country: Number of subjects enrolled	United States: 32
Worldwide total number of subjects	100
EEA total number of subjects	53

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)	28
From 65 to 84 years	69
85 years and over	3

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 38 investigative sites in the United States, Belgium, Ukraine, the Czech Republic, Hungary, Bulgaria, Italy, Poland, and Switzerland from 05 June 2016 to 25 June 2021.

Pre-assignment

Screening details:

A total of 127 subjects were screened and 100 subjects with relapsed or refractory (r/r) diffuse large B-cell lymphoma (DLBCL) and other forms of non-Hodgkin's lymphoma (NHL) were enrolled, 37 subjects into Part 1 and 63 subjects into Part 2/3.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Part 1: Safety Run-in

Arm description:

Subjects received Debio 1562 0.7 mg/kg, intravenous (IV) infusion followed by rituximab 375 mg/m^2 IV infusion, once on Day 1 of 21-day cycles until the study discontinuation criteria were met (until they develop disease progression, death, unacceptable toxicity, withdraw consent, start new anti-lymphoma treatment or the Sponsor terminates the study).

Arm type	Experimental
Investigational medicinal product name	Debio 1562
Investigational medicinal product code	
Other name	Naratuximab emtansine, IMGN529
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

0.7 mg/kg IV infusion

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

Dosage and administration details:

375 mg/m^2 IV infusion

Arm title	Part 1: Cohort 1

Arm description:

Subjects with R/R DLBCL received Debio 1562 0.7 mg/kg, IV infusion followed by rituximab 375 mg/m^2 IV infusion, once on Day 1 of 21-day cycles until the study discontinuation criteria were met (until they develop disease progression, death, unacceptable toxicity, withdraw consent, start new anti-lymphoma treatment or the Sponsor terminates the study).

Arm type	Experimental
Investigational medicinal product name	Debio 1562
Investigational medicinal product code	
Other name	Naratuximab emtansine, IMGN529
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details: 0.7 mg/kg IV infusion	
Investigational medicinal product name	Rituximab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: 375 mg/m^2 IV infusion	
Arm title	Part 1: Cohort 2

Arm description:

Subjects with R/R NHL received Debio 1562 0.7 mg/kg, IV infusion followed by rituximab 375 mg/m^2 IV infusion, once on Day 1 of 21-day cycles until the study discontinuation criteria were met (until they develop disease progression, death, unacceptable toxicity, withdraw consent, start new anti-lymphoma treatment or the Sponsor terminates the study).

Arm type	Experimental
Investigational medicinal product name	Debio 1562
Investigational medicinal product code	
Other name	Naratuximab emtansine, IMGN529
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: 0.7 mg/kg IV infusion	
Investigational medicinal product name	Rituximab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: 375 mg/m^2 IV infusion	
Arm title	Part 2/3: Cohort A

Arm description:

Subjects with relapsed DLBCL received Debio 1562 0.7 mg/kg, IV infusion followed by rituximab 375 mg/m^2 IV infusion, once on Day 1 of a 21-day cycle for at least 6 cycles.

Arm type	Experimental
Investigational medicinal product name	Debio 1562
Investigational medicinal product code	
Other name	Naratuximab emtansine, IMGN529
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: 0.7 mg/kg IV infusion	
Investigational medicinal product name	Rituximab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: 375 mg/m^2 IV infusion	
Arm title	Part 2/3: Cohort B

Arm description:

Subjects with relapsed DLBCL received Debio 1562 0.4 mg/kg IV infusion followed by rituximab 375

mg/m^2 IV infusion on Day 1, then Debio 1562 0.2 mg/kg IV infusion on Days 8 and 15 of a 21-day cycle for at least 6 cycles.

Arm type	Experimental
Investigational medicinal product name	Debio 1562
Investigational medicinal product code	
Other name	Naratuximab emtansine, IMGN529
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

0.2 and 0.4 mg/kg IV infusion

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

Dosage and administration details:

375 mg/m^2 IV infusion

Number of subjects in period 1	Part 1: Safety Run-in	Part 1: Cohort 1	Part 1: Cohort 2
Started	17	8	12
Completed	5	1	4
Not completed	12	7	8
Subject Withdrew Consent	1	1	1
Death	10	5	4
Investigator decision	-	-	-
Reason not specified	1	-	-
Lost to follow-up	-	1	-
End of Study Page Missing	-	-	3

Number of subjects in period 1	Part 2/3: Cohort A	Part 2/3: Cohort B
Started	33	30
Completed	14	10
Not completed	19	20
Subject Withdrew Consent	-	2
Death	16	16
Investigator decision	-	1
Reason not specified	-	-
Lost to follow-up	-	1
End of Study Page Missing	3	-

Baseline characteristics

Reporting groups	
Reporting group title	Part 1: Safety Run-in
Reporting group description:	
Subjects received Debio 1562 0.7 mg/kg, intravenous (IV) infusion followed by rituximab 375 mg/m^2 IV infusion, once on Day 1 of 21-day cycles until the study discontinuation criteria were met (until they develop disease progression, death, unacceptable toxicity, withdraw consent, start new anti-lymphoma treatment or the Sponsor terminates the study).	
Reporting group title	Part 1: Cohort 1
Reporting group description:	
Subjects with R/R DLBCL received Debio 1562 0.7 mg/kg, IV infusion followed by rituximab 375 mg/m^2 IV infusion, once on Day 1 of 21-day cycles until the study discontinuation criteria were met (until they develop disease progression, death, unacceptable toxicity, withdraw consent, start new anti-lymphoma treatment or the Sponsor terminates the study).	
Reporting group title	Part 1: Cohort 2
Reporting group description:	
Subjects with R/R NHL received Debio 1562 0.7 mg/kg, IV infusion followed by rituximab 375 mg/m^2 IV infusion, once on Day 1 of 21-day cycles until the study discontinuation criteria were met (until they develop disease progression, death, unacceptable toxicity, withdraw consent, start new anti-lymphoma treatment or the Sponsor terminates the study).	
Reporting group title	Part 2/3: Cohort A
Reporting group description:	
Subjects with relapsed DLBCL received Debio 1562 0.7 mg/kg, IV infusion followed by rituximab 375 mg/m^2 IV infusion, once on Day 1 of a 21-day cycle for at least 6 cycles.	
Reporting group title	Part 2/3: Cohort B
Reporting group description:	
Subjects with relapsed DLBCL received Debio 1562 0.4 mg/kg IV infusion followed by rituximab 375 mg/m^2 IV infusion on Day 1, then Debio 1562 0.2 mg/kg IV infusion on Days 8 and 15 of a 21-day cycle for at least 6 cycles.	

Reporting group values	Part 1: Safety Run-in	Part 1: Cohort 1	Part 1: Cohort 2
Number of subjects	17	8	12
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	68.5	70.1	68.5
standard deviation	± 13.05	± 9.79	± 5.92
Gender categorical Units: Subjects			
Female	5	5	5
Male	12	3	7
Ethnicity Units: Subjects			
Hispanic or Latino	1	1	0
Not Hispanic or Latino	15	5	12
Not Reported	1	2	0
Race Units: Subjects			
White	16	7	11

African American	0	0	0
Asian	1	0	1
Not Reported	0	1	0
Other	0	0	0

Reporting group values	Part 2/3: Cohort A	Part 2/3: Cohort B	Total
Number of subjects	33	30	100
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	65.7	68.7	
standard deviation	± 13.26	± 11.78	-
Gender categorical Units: Subjects			
Female	14	15	44
Male	19	15	56
Ethnicity Units: Subjects			
Hispanic or Latino	1	2	5
Not Hispanic or Latino	32	28	92
Not Reported	0	0	3
Race Units: Subjects			
White	31	30	95
African American	1	0	1
Asian	0	0	2
Not Reported	0	0	1
Other	1	0	1

End points

End points reporting groups

Reporting group title	Part 1: Safety Run-in

Reporting group description:

Subjects received Debio 1562 0.7 mg/kg, intravenous (IV) infusion followed by rituximab 375 mg/m^2 IV infusion, once on Day 1 of 21-day cycles until the study discontinuation criteria were met (until they develop disease progression, death, unacceptable toxicity, withdraw consent, start new anti-lymphoma treatment or the Sponsor terminates the study).

Reporting group title	Part 1: Cohort 1

Reporting group description:

Subjects with R/R DLBCL received Debio 1562 0.7 mg/kg, IV infusion followed by rituximab 375 mg/m^2 IV infusion, once on Day 1 of 21-day cycles until the study discontinuation criteria were met (until they develop disease progression, death, unacceptable toxicity, withdraw consent, start new anti-lymphoma treatment or the Sponsor terminates the study).

Reporting group title	Part 1: Cohort 2

Reporting group description:

Subjects with R/R NHL received Debio 1562 0.7 mg/kg, IV infusion followed by rituximab 375 mg/m^2 IV infusion, once on Day 1 of 21-day cycles until the study discontinuation criteria were met (until they develop disease progression, death, unacceptable toxicity, withdraw consent, start new anti-lymphoma treatment or the Sponsor terminates the study).

Reporting group title	Part 2/3: Cohort A

Reporting group description:

Subjects with relapsed DLBCL received Debio 1562 0.7 mg/kg, IV infusion followed by rituximab 375 mg/m^2 IV infusion, once on Day 1 of a 21-day cycle for at least 6 cycles.

Reporting group title	Part 2/3: Cohort B

Reporting group description:

Subjects with relapsed DLBCL received Debio 1562 0.4 mg/kg IV infusion followed by rituximab 375 mg/m^2 IV infusion on Day 1, then Debio 1562 0.2 mg/kg IV infusion on Days 8 and 15 of a 21-day cycle for at least 6 cycles.

Primary: Number of Subjects With Treatment-emergent Adverse Events (TEAEs)

End point title	Number of Subjects With Treatment-emergent Adverse Events (TEAEs)[1]

End point description:

An AE was defined as any noxious, pathologic, or unintended change in anatomical, physiologic, or metabolic function as indicated by physical signs, symptoms, or laboratory changes occurring in any phase of a clinical study, whether or not considered study drug related. This included exacerbation of a pre-existing condition. AEs included worsening (change in nature, severity, or frequency) of conditions present at the onset of the study, intercurrent illnesses, drug interactions, events related to or possibly related to concomitant medications, abnormal laboratory values (this included significant shifts from baseline within the range of normal that the Investigator considered to be clinically important), clinically significant abnormalities in physical examination, vital signs, and weight. Safety population included all subjects from the screened population who received at least one dose of Debio 1562.

End point type	Primary

End point timeframe:

Up to 30 days after end of treatment (EOT) (Up to 38 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 statistical analysis was planned to be reported for this endpoint.

End point values	Part 1: Safety Run-in	Part 1: Cohort 1	Part 1: Cohort 2	Part 2/3: Cohort A
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	8	12	33
Units: subjects with any TEAEs	16	8	12	32

End point values	Part 2/3: Cohort B			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: subjects with any TEAEs	29			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Clinically Significant Changes in Clinical Laboratory Test Results Reported as TEAEs

End point title	Number of Subjects With Clinically Significant Changes in Clinical Laboratory Test Results Reported as TEAEs[2]

End point description:

The clinical laboratory tests included Hematology: Hematocrit (Hct),hemoglobin (Hgb),platelet count, red blood cell (RBC) count, white blood cell (WBC) count with differential; Serum Chemistry: Albumin (ALB),alkaline phosphatase(ALK-P),alanine aminotransferase(ALT), serum glutamic pyruvic transaminase; (SGPT), aspartate aminotransferase (AST), serum glutamic oxaloacetic transaminase (SGOT),blood urea nitrogen (BUN),calcium(Ca),chloride(Cl),creatinine, glucose, lactate dehydrogenase(LDH),magnesium, phosphorus, potassium(K),sodium(Na),total bilirubin, total protein, uric acid, immunoglobulin levels(IgG, IgA, IgM); Urinalysis: Appearance, specific gravity and pH, evaluation of glucose, protein, bilirubin, ketones, leukocytes and blood; Coagulation: Prothrombin time(PT) or international normalized ratio(INR),activated partial thromboplastin time(aPTT). Safety population= all subjects from the screened population who received at least one dose of Debio 1562.

End point type	Primary

End point timeframe:

Up to 30 days after EOT (Up to 38 months)

Notes:

[2] - 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 statistical analysis was planned to be reported for this endpoint.

End point values	Part 1: Safety Run-in	Part 1: Cohort 1	Part 1: Cohort 2	Part 2/3: Cohort A
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	8	12	33
Units: subjects				
Neutrophil Count Decreased	6	1	2	2
Lymphocyte Count Decreased	5	1	0	0
WBC Count Decreased	5	0	0	1
Platelet Count Decreased	4	1	3	0
Anaemia	0	2	2	7
Leukopenia	0	1	1	5
Neutropenia	1	1	4	21

Lymphopenia	0	0	0	8
Hypophosphataemia	1	0	1	1
Thrombocytopenia	0	1	1	4
Febrile Neutropenia	2	0	1	1
AST Increased	2	2	1	0
ALK-P Increased	3	0	1	1
ALT Increased	2	1	0	1
Blood Creatinine Increased	0	1	1	1
Hemoglobin Decreased	2	0	0	0
Blood Immunoglobulin G Decreased	0	0	0	1
Blood Magnesium Decreased	0	0	0	0
Hyperkalaemia	1	1	2	0
Hypoalbuminaemia	0	0	0	2
Hypercalcaemia	1	0	0	2
Hyperglycaemia	0	0	0	2
Hypernatraemia	0	0	1	0
Hyponatraemia	2	0	0	0
Hyperphosphataemia	0	0	0	0
Hyperuricaemia	0	0	1	1
Hypoglycaemia	1	0	1	0
Hypomagnesaemia	0	0	1	1
Blood Bilirubin Increased	1	0	0	1
Hypokalaemia	2	0	2	0
Gamma-glutamyl transferase Increased	0	0	0	2

End point values	Part 2/3: Cohort B			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: subjects				
Neutrophil Count Decreased	2			
Lymphocyte Count Decreased	0			
WBC Count Decreased	3			
Platelet Count Decreased	2			
Anaemia	6			
Leukopenia	7			
Neutropenia	17			
Lymphopenia	6			
Hypophosphataemia	0			
Thrombocytopenia	6			
Febrile Neutropenia	1			
AST Increased	1			
ALK-P Increased	1			
ALT Increased	1			
Blood Creatinine Increased	0			
Hemoglobin Decreased	0			
Blood Immunoglobulin G Decreased	1			
Blood Magnesium Decreased	0			
Hyperkalaemia	2			

Hypoalbuminaemia	0			
Hypercalcaemia	1			
Hyperglycaemia	0			
Hypernatraemia	1			
Hyponatraemia	1			
Hyperphosphataemia	0			
Hyperuricaemia	0			
Hypoglycaemia	0			
Hypomagnesaemia	0			
Blood Bilirubin Increased	0			
Hypokalaemia	2			
Gamma-glutamyl transferase Increased	1			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Clinically Significant Changes in Electrocardiogram (ECG) Reported as TEAEs

End point title	Number of Subjects With Clinically Significant Changes in Electrocardiogram (ECG) Reported as TEAEs[3]

End point description:

A standard 12-lead ECG was performed. Safety population included all subjects from the screened population who received at least one dose of Debio 1562.

End point type	Primary

End point timeframe:

Up to 30 days after EOT (Up to 38 months)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive statistical analysis was planned to be reported for this endpoint.

End point values	Part 1: Safety Run-in	Part 1: Cohort 1	Part 1: Cohort 2	Part 2/3: Cohort A
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	8	12	33
Units: subjects				
Atrial Fibrillation	0	0	1	0
Electrocardiogram QT prolonged	0	0	0	1
Acute myocardial infarction	1	0	1	0

End point values	Part 2/3: Cohort B			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: subjects				
Atrial Fibrillation	1			
Electrocardiogram QT prolonged	1			

Acute myocardial infarction	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Clinically Significant Changes in Vital Sign Measurements Reported as TEAEs

End point title	Number of Subjects With Clinically Significant Changes in Vital Sign Measurements Reported as TEAEs[4]

End point description:

Vital signs included systolic and diastolic blood pressure, heart rate, temperature, and respiratory rate. Safety population included all subjects from the screened population who received at least one dose of Debio 1562.

End point type	Primary

End point timeframe:

Up to 30 days after EOT (Up to 38 months)

Notes:

[4] - 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 statistical analysis was planned to be reported for this endpoint.

End point values	Part 1: Safety Run-in	Part 1: Cohort 1	Part 1: Cohort 2	Part 2/3: Cohort A
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	8	12	33
Units: subjects				
Body Temperature Increased	1	0	0	1
Hypertension	0	0	0	3
Hypotension	0	0	1	1
Pyrexia	4	2	1	6
Hyperthermia	0	0	0	0
Tachycardia	1	0	0	0

End point values	Part 2/3: Cohort B			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: subjects				
Body Temperature Increased	0			
Hypertension	2			
Hypotension	0			
Pyrexia	4			
Hyperthermia	2			
Tachycardia	1			

Statistical analyses

No statistical analyses for this end point

Primary: Objective Response Rate (ORR)

End point title	Objective Response Rate (ORR)[5]

End point description:

ORR was defined as the percentage of subjects with a Best overall response (BOR) of partial response (PR) or complete response (CR). BOR was the best response recorded from the start of the treatment until disease progression, initiation of new anti-cancer therapy, or end of the study period, whichever occurred first. CR was defined as disappearance of all target lesions, no new lesions formation. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to ≤1.5 cm. PR was defined as ≥50% decrease in the sum of diameters of up to 6 target measurable nodes or extranodal sites, no new lesions formation. Efficacy Evaluable (EE) population included all subjects who received at least one dose of Debio 1562 and rituximab and had both baseline and post-baseline evaluable disease assessments (including clinical progressive disease [PD]).

End point type	Primary

End point timeframe:

Up to PD or death or end of study (approximately 57 months) or initiation of new anti-cancer therapy whichever occurs first

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analysis data was provided as an attachment due to database constraints.

End point values	Part 1: Safety Run-in	Part 1: Cohort 1	Part 1: Cohort 2	Part 2/3: Cohort A
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	8	11	30
Units: percent responders				
number (confidence interval 95%)	26.7 (7.8 to 55.1)	12.5 (0.3 to 52.7)	81.8 (48.2 to 97.7)	50.0 (31.3 to 68.7)

End point values	Part 2/3: Cohort B			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: percent responders				
number (confidence interval 95%)	50.0 (31.3 to 68.7)			

Attachments (see zip file)	Objective Response Rate -Statistical analysis data/Objective

Statistical analyses

No statistical analyses for this end point

Secondary: PK Parameter: Maximum Plasma Concentration (Cmax) of Debio 1562 and Rituximab

End point title	PK Parameter: Maximum Plasma Concentration (Cmax) of Debio 1562 and Rituximab

End point description:

PK population included all subjects who received at least one dose of Debio 1562 or rituximab and had atleast one PK concentration result available. Number analysed signifies the number of participants with available data at the specific timepoint. 99999= Data cannot be calculated due to low number of events.

End point type	Secondary

End point timeframe:

Parts 1, 2/3: Pre-dose, post infusion-5 min on Day 1 of Cycles (C) 1-6, 5 min on Day 1 of C7, 8 and 2 h on Day 1 of C1, 2 (only for Part 2/3), 24 h on Day 2, 48 h on Day 3, Days 8 and 15 of C1, 2 (Cycle=21 days); EOT (up to 38 months), 30-day follow up

End point values	Part 1: Safety Run-in	Part 1: Cohort 1	Part 1: Cohort 2	Part 2/3: Cohort A
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	8	12	32
Units: nanogram per milliliter (ng/ml)				
arithmetic mean (standard deviation)				
Debio 1562: Cycle 1 (n=17,8,12,32,29)	10005.9 (± 4147.35)	9411.5 (± 7762.98)	11821.2 (± 5456.11)	15339.4 (± 3514.51)
Debio 1562: Cycle 2 (n=14,6,7,29,24)	8697.9 (± 3540.53)	7775.0 (± 2646.11)	10521.4 (± 3448.39)	13868.6 (± 4143.59)
Debio 1562: Cycle 3 (n=10,4,9,18,19)	10600.0 (± 3879.40)	11472.5 (± 3684.63)	13682.2 (± 3093.84)	14324.4 (± 5532.63)
Debio 1562: Cycle 4 (n=9,3,9,16,17)	7787.8 (± 3334.11)	9230.0 (± 1980.08)	11703.3 (± 2284.15)	12560.0 (± 4625.17)
Debio 1562: Cycle 5 (n=7,2,8,14,16)	9744.3 (± 1816.91)	9675.0 (± 1308.15)	13220.0 (± 2049.06)	13487.1 (± 4458.46)
Debio 1562: Cycle 6 (n=6,2,8,14,14)	8050.0 (± 2418.64)	10195.0 (± 3825.45)	12983.8 (± 3182.10)	13025.7 (± 5043.89)
Debio 1562: Cycle 7 (n=5,1,7,0,0)	7908.0 (± 3111.60)	9940.0 (± 99999)	12600.0 (± 1803.70)	99999 (± 99999)
Debio 1562: Cycle 8 (n=3,0,8,0,0)	2253.0 (± 2214.31)	99999 (± 99999)	12501.3 (± 2658.79)	99999 (± 99999)
Debio 1562: Cycle 999 (n=0,0,0,0,1)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Rituximab: Cycle 1 (n=16,8,12,32,29)	213287.4 (± 55735.54)	207415.8 (± 67408.74)	179430.7 (± 41213.48)	170942.3 (± 28871.50)
Rituximab: Cycle 2 (n=14,7,11,29,24)	251697.6 (± 41113.07)	214761.9 (± 40919.84)	191988.5 (± 65788.33)	205481.9 (± 43738.73)
Rituximab: Cycle 3 (n=9,4,9,18,18)	272302.8 (± 58497.66)	213378.8 (± 36470.96)	239380.8 (± 60127.34)	218358.1 (± 49891.16)
Rituximab: Cycle 4 (n=8,3,9,16,17)	283067.9 (± 57414.89)	198313.3 (± 79455.19)	262263.9 (± 67895.19)	236146.8 (± 63699.49)
Rituximab: Cycle 5 (n=7,2,8,14,15)	366032.9 (± 94593.53)	156582.0 (± 82703.21)	266406.1 (± 52480.70)	282017.6 (± 66512.79)
Rituximab: Cycle 6 (n=6,2,8,14,14)	354142.7 (± 90095.73)	200913.0 (± 130086.43)	240735.0 (± 114120.93)	294989.5 (± 82301.31)
Rituximab: Cycle 7 (n=5,1,7,1,0)	341761.4 (± 37261.58)	179381.0 (± 99999)	281045.9 (± 62528.32)	251289.3 (± 81723.02)

Rituximab: Cycle 8 (n=3,0,8,0,0)	379038.7 (± 83552.42)	99999 (± 99999)	251326.4 (± 85797.08)	99999 (± 99999)
Rituximab: Cycle 888 (n=9,4,8,13,14)	77330.7 (± 34343.07)	59503.5 (± 9683.76)	53960.9 (± 61954.05)	86046.4 (± 53904.82)
Rituximab: Cycle 999 (n=12,5,7,20,20)	107690.6 (± 56044.52)	82585.0 (± 31312.62)	78777.3 (± 72013.43)	69646.9 (± 49779.31)

End point values	Part 2/3: Cohort B			
Subject group type	Reporting group			
Number of subjects analysed	29			
Units: nanogram per milliliter (ng/ml)				
arithmetic mean (standard deviation)				
Debio 1562: Cycle 1 (n=17,8,12,32,29)	6612.4 (± 2315.16)			
Debio 1562: Cycle 2 (n=14,6,7,29,24)	8465.5 (± 6553.50)			
Debio 1562: Cycle 3 (n=10,4,9,18,19)	6824.0 (± 2911.62)			
Debio 1562: Cycle 4 (n=9,3,9,16,17)	7122.9 (± 3084.39)			
Debio 1562: Cycle 5 (n=7,2,8,14,16)	7305.0 (± 3089.01)			
Debio 1562: Cycle 6 (n=6,2,8,14,14)	6904.3 (± 2516.11)			
Debio 1562: Cycle 7 (n=5,1,7,0,0)	99999 (± 99999)			
Debio 1562: Cycle 8 (n=3,0,8,0,0)	99999 (± 99999)			
Debio 1562: Cycle 999 (n=0,0,0,0,1)	15000.0 (± 99999)			
Rituximab: Cycle 1 (n=16,8,12,32,29)	171006.4 (± 37226.83)			
Rituximab: Cycle 2 (n=14,7,11,29,24)	210563.7 (± 43723.39)			
Rituximab: Cycle 3 (n=9,4,9,18,18)	254760.9 (± 107449.36)			
Rituximab: Cycle 4 (n=8,3,9,16,17)	267141.2 (± 65390.99)			
Rituximab: Cycle 5 (n=7,2,8,14,15)	267163.1 (± 51180.64)			
Rituximab: Cycle 6 (n=6,2,8,14,14)	296240.1 (± 68962.34)			
Rituximab: Cycle 7 (n=5,1,7,1,0)	99999 (± 99999)			
Rituximab: Cycle 8 (n=3,0,8,0,0)	99999 (± 99999)			
Rituximab: Cycle 888 (n=9,4,8,13,14)	73469.1 (± 47009.66)			
Rituximab: Cycle 999 (n=12,5,7,20,20)	79561.6 (± 55656.86)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)

End point description:

PFS was defined as the duration between the first dose date of Debio 1562 and the date of progressive disease (PD) or death due to any cause, whichever occurs first. PD is defined as the new or clear progression of preexisting non-measured lesions or regrowth of previously resolved lesions or a new node >1.5 cm in any axis or an abnormal lesion with >1.5 cm longest transverse diameter or increase by >50% of lesion. EE population included all subjects who received at least one dose of Debio 1562 and rituximab and had both baseline and post-baseline evaluable disease assessments (including clinical PD). 99999=Data is not available due to low number of events.

End point type	Secondary

End point timeframe:

Up to PD or death or end of study (approximately 57 months) or initiation of new anti-cancer therapy whichever occurs first

End point values	Part 1: Safety Run-in	Part 1: Cohort 1	Part 1: Cohort 2	Part 2/3: Cohort A
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	8	11	30
Units: months				
median (confidence interval 95%)	1.4 (1.2 to 11.1)	1.8 (1.3 to 4.0)	20.7 (10.5 to 99999)	5.1 (1.4 to 99999)

End point values	Part 2/3: Cohort B			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: months				
median (confidence interval 95%)	4.6 (1.4 to 13.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Response (TTR)

End point title	Time to Response (TTR)

End point description:

TTR was defined as the duration between the first dose date of Debio 1562 and the date of first objective response (PR or CR). CR was defined as disappearance of all target lesions, no new lesions formation. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to ≤ 1.5 cm. PR was defined as ≥50% decrease in the sum of diameters of up to 6 target measurable nodes or extranodal sites, no new lesions formation. EE population included all subjects who received at least one dose of Debio 1562 and rituximab and had both baseline and post-baseline evaluable disease assessments (including clinical PD). Data is reported only for participants who responded. 99999= Data is not available due to low number of subjects with events.

End point type	Secondary

End point timeframe:

Up to PD or death or end of study (approximately 57 months) or initiation of new anti-cancer therapy whichever occurs first

End point values	Part 1: Safety Run-in	Part 1: Cohort 1	Part 1: Cohort 2	Part 2/3: Cohort A
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	1	9	15
Units: months				
median (confidence interval 95%)	1.4 (1.2 to 99999)	1.4 (0.0 to 99999)	1.4 (1.4 to 2.1)	1.5 (1.4 to 1.8)

End point values	Part 2/3: Cohort B			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: months				
median (confidence interval 95%)	1.5 (1.4 to 3.3)			

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 was defined as duration between date of the first objective response (PR or CR) and date of PD or death due to any cause, whichever occurs first. CR: Disappearance of all target lesions, no new lesions formation, any pathological lymph nodes (whether target or non-target) must have reduction in short axis to ≤1.5 cm. PR: ≥50% decrease in sum of diameters of up to 6 target measurable nodes or extranodal sites, no new lesions formation. PD: New or clear progression of preexisting non-measured lesions or regrowth of previously resolved lesions or a new node >1.5 cm in any axis or an abnormal lesion with >1.5 cm longest transverse diameter or increase by >50% of lesion. EE population included all subjects who received at least one dose of Debio 1562 and rituximab and had both baseline and post-baseline evaluable disease assessments (including clinical PD). Data is reported only for subjects who responded. 99999=Data is not available due to low number of events.

End point type	Secondary

End point timeframe:

Up to PD or death or end of study (approximately 57 months) or initiation of new anti-cancer therapy whichever occurs first

End point values	Part 1: Safety Run-in	Part 1: Cohort 1	Part 1: Cohort 2	Part 2/3: Cohort A
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	1	9	15
Units: months				
median (confidence interval 95%)	99999 (9.7 to 99999)	2.6 (0.0 to 99999)	99999 (13.2 to 99999)	99999 (13.6 to 99999)

End point values	Part 2/3: Cohort B			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: months				
median (confidence interval 95%)	16.5 (3.4 to 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

OS was defined as the duration between the first dose date of Debio 1562 and the date of death due to any cause. EE population included all subjects who received at least one dose of Debio 1562 and rituximab and had both baseline and post-baseline evaluable disease assessments (including clinical PD). 99999= Data is not available due to low number of subjects with events.

End point type	Secondary

End point timeframe:

Up to death or end of study (approximately 57 months) or one year from the last participant`s first dose

End point values	Part 1: Safety Run-in	Part 1: Cohort 1	Part 1: Cohort 2	Part 2/3: Cohort A
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	8	11	30
Units: months				
median (confidence interval 95%)	30.0 (13.3 to 99999)	8.4 (2.7 to 17.0)	34.3 (24.3 to 99999)	99999 (11.4 to 99999)

End point values	Part 2/3: Cohort B			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: months				

median (confidence interval 95%)	17.3 (9.5 to 99999)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All-cause mortality: Up to end of study (approximately 57 months); Adverse events: Up to 30 days after EOT (Up to 38 months)

Adverse event reporting additional description:

Safety Population included all subjects from the screened population who received at least 1 dose of Debio 1562.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	Part 1: Safety Run-in

Reporting group description:

Subjects received Debio 1562 0.7 mg/kg, IV infusion followed by rituximab 375 mg/m^2 IV infusion, once on Day 1 of 21-day cycles until the study discontinuation criteria were met (until they develop disease progression, death, unacceptable toxicity, withdraw consent, start new anti-lymphoma treatment or the Sponsor terminates the study).

Reporting group title	Part 1: Cohort 1

Reporting group description:

Subjects with R/R DLBCL received Debio 1562 0.7 mg/kg, IV infusion followed by rituximab 375 mg/m^2 IV infusion, once on Day 1 of 21-day cycles until the study discontinuation criteria were met (until they develop disease progression, death, unacceptable toxicity, withdraw consent, start new anti-lymphoma treatment or the Sponsor terminates the study).

Reporting group title	Part 1: Cohort 2

Reporting group description:

Subjects with R/R NHL received Debio 1562 0.7 mg/kg, IV infusion followed by rituximab 375 mg/m^2 IV infusion, once on Day 1 of 21-day cycles until the study discontinuation criteria were met (until they develop disease progression, death, unacceptable toxicity, withdraw consent, start new anti-lymphoma treatment or the Sponsor terminates the study).

Reporting group title	Part 2/3: Cohort A

Reporting group description:

Subjects with relapsed DLBCL received Debio 1562 0.7 mg/kg, IV infusion followed by rituximab 375 mg/m^2 IV infusion, once on Day 1 of a 21-day cycle for at least 6 cycles.

Reporting group title	Part 2/3: Cohort B

Reporting group description:

Subjects with relapsed DLBCL received Debio 1562 0.4 mg/kg IV infusion followed by rituximab 375 mg/m^2 IV infusion on Day 1, then Debio 1562 0.2 mg/kg IV infusion on Days 8 and 15 of a 21-day cycle for at least 6 cycles.

Serious adverse events	Part 1: Safety Run-in	Part 1: Cohort 1	Part 1: Cohort 2
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 17 (29.41%)	3 / 8 (37.50%)	5 / 12 (41.67%)
number of deaths (all causes)	11	6	5
number of deaths resulting from adverse events	1	0	2
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Adenocarcinoma of colon			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Intraductal papillary mucinous neoplasm			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 12 (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
Tumour pain			
subjects affected / exposed	0 / 17 (0.00%)	1 / 8 (12.50%)	0 / 12 (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
Vascular disorders			
Aortic stenosis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Circulatory collapse			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 12 (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			
General physical health deterioration			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 12 (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
Pyrexia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 12 (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 / 17 (0.00%)	0 / 8 (0.00%)	0 / 12 (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
Reproductive system and breast disorders			
Prostatitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 12 (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
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 12 (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
Pneumonitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 12 (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
Pulmonary embolism			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 12 (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
Respiratory failure			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 12 (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
Sinus pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Humerus fracture			

subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 12 (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
Infusion related reaction			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 12 (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
Post procedural fever			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 12 (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	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 12 (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 arrest			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 12 (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 failure chronic			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 12 (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
Coronary artery disease			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Left ventricular failure			

subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 12 (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	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 12 (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
Hypoglycaemic seizure			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
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			
Febrile neutropenia			
subjects affected / exposed	2 / 17 (11.76%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	1 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 12 (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			
Dysphagia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 12 (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
Oral pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 12 (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

Rectal haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 12 (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
Hepatobiliary disorders			
Hepatitis toxic			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 12 (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 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Haematuria			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 12 (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
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 17 (0.00%)	1 / 8 (12.50%)	0 / 12 (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
Chondrocalcinosis pyrophosphate			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 12 (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
Osteoarthritis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 12 (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
Soft tissue mass			

subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 12 (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
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 8 (12.50%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 12 (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
Influenza			
subjects affected / exposed	0 / 17 (0.00%)	1 / 8 (12.50%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 17 (0.00%)	1 / 8 (12.50%)	0 / 12 (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
COVID-19 pneumonia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 12 (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
Cellulitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			

subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 12 (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
Gangrene			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 12 (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
Sinusitis aspergillus			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypercalcaemia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 12 (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

Serious adverse events	Part 2/3: Cohort A	Part 2/3: Cohort B	
Total subjects affected by serious adverse events			
subjects affected / exposed	15 / 33 (45.45%)	9 / 30 (30.00%)	
number of deaths (all causes)	16	17	
number of deaths resulting from adverse events	5	2	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intraductal papillary mucinous neoplasm			
subjects affected / exposed	0 / 33 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour pain			

subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aortic stenosis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Circulatory collapse			
subjects affected / exposed	1 / 33 (3.03%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
General physical health deterioration			
subjects affected / exposed	3 / 33 (9.09%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pyrexia			
subjects affected / exposed	2 / 33 (6.06%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 33 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Reproductive system and breast disorders			
Prostatitis			
subjects affected / exposed	0 / 33 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			

subjects affected / exposed	0 / 33 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	1 / 33 (3.03%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	1 / 33 (3.03%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Sinus pain			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Humerus fracture			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infusion related reaction			
subjects affected / exposed	1 / 33 (3.03%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural fever			
subjects affected / exposed	0 / 33 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			

Acute myocardial infarction			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	0 / 33 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	1 / 33 (3.03%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac failure chronic			
subjects affected / exposed	0 / 33 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Coronary artery disease			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left ventricular failure			
subjects affected / exposed	1 / 33 (3.03%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemic seizure			

subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	1 / 33 (3.03%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia			
subjects affected / exposed	0 / 33 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Dysphagia			
subjects affected / exposed	1 / 33 (3.03%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral pain			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	1 / 33 (3.03%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatitis toxic			
subjects affected / exposed	1 / 33 (3.03%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			

subjects affected / exposed	1 / 33 (3.03%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	0 / 33 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chondrocalcinosis pyrophosphate			
subjects affected / exposed	1 / 33 (3.03%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	0 / 33 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Soft tissue mass			
subjects affected / exposed	1 / 33 (3.03%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 33 (3.03%)	2 / 30 (6.67%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	1 / 33 (3.03%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

COVID-19			
subjects affected / exposed	1 / 33 (3.03%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Influenza			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 33 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19 pneumonia			
subjects affected / exposed	0 / 33 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	1 / 33 (3.03%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gangrene			
subjects affected / exposed	0 / 33 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinusitis aspergillus			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			

Hypercalcaemia			
subjects affected / exposed	1 / 33 (3.03%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Part 1: Safety Run-in	Part 1: Cohort 1	Part 1: Cohort 2
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 17 (88.24%)	8 / 8 (100.00%)	12 / 12 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant muscle neoplasm			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Seborrhoeic keratosis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Tumour pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Flushing			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	0	2
Hot flush			
subjects affected / exposed	1 / 17 (5.88%)	1 / 8 (12.50%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
Hypotension			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Lymphostasis			

subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Cyanosis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Deep vein thrombosis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Phlebitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	8 / 17 (47.06%)	1 / 8 (12.50%)	4 / 12 (33.33%)
occurrences (all)	8	1	10
Pyrexia			
subjects affected / exposed	4 / 17 (23.53%)	2 / 8 (25.00%)	1 / 12 (8.33%)
occurrences (all)	5	3	1
Asthenia			
subjects affected / exposed	1 / 17 (5.88%)	1 / 8 (12.50%)	4 / 12 (33.33%)
occurrences (all)	2	2	4
Oedema peripheral			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	4 / 12 (33.33%)
occurrences (all)	0	0	10
Chills			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	2 / 12 (16.67%)
occurrences (all)	1	0	2
Non-cardiac chest pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Hyperthermia			

subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	2 / 17 (11.76%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
Chest pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Facial pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Swelling			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	6 / 17 (35.29%)	2 / 8 (25.00%)	6 / 12 (50.00%)
occurrences (all)	12	3	11
Dyspnoea			
subjects affected / exposed	3 / 17 (17.65%)	1 / 8 (12.50%)	5 / 12 (41.67%)
occurrences (all)	6	1	10
Nasal congestion			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	2 / 12 (16.67%)
occurrences (all)	1	0	2
Oropharyngeal pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Pleural effusion			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Rhinorrhoea			

subjects affected / exposed	2 / 17 (11.76%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	3	0	0
Hypoxia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Pharyngeal erythema			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Productive cough			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Pulmonary mass			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Stridor			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Psychiatric disorders			
Insomnia			
subjects affected / exposed	3 / 17 (17.65%)	0 / 8 (0.00%)	2 / 12 (16.67%)
occurrences (all)	4	0	7
Anxiety			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	2 / 12 (16.67%)
occurrences (all)	1	0	2
Confusional state			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Investigations			
Neutrophil count decreased			
subjects affected / exposed	6 / 17 (35.29%)	1 / 8 (12.50%)	2 / 12 (16.67%)
occurrences (all)	18	1	4
Lymphocyte count decreased			
subjects affected / exposed	5 / 17 (29.41%)	1 / 8 (12.50%)	0 / 12 (0.00%)
occurrences (all)	23	1	0
White blood cell count decreased			

subjects affected / exposed	5 / 17 (29.41%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	18	0	0
Platelet count decreased			
subjects affected / exposed	4 / 17 (23.53%)	1 / 8 (12.50%)	3 / 12 (25.00%)
occurrences (all)	6	1	7
Alanine aminotransferase increased			
subjects affected / exposed	2 / 17 (11.76%)	1 / 8 (12.50%)	0 / 12 (0.00%)
occurrences (all)	4	2	0
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 17 (11.76%)	2 / 8 (25.00%)	1 / 12 (8.33%)
occurrences (all)	2	3	1
Blood alkaline phosphatase increased			
subjects affected / exposed	3 / 17 (17.65%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	3	0	1
Weight decreased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Blood creatinine increased			
subjects affected / exposed	0 / 17 (0.00%)	1 / 8 (12.50%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin increased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Body temperature increased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Haemoglobin decreased			
subjects affected / exposed	2 / 17 (11.76%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	4	0	0
Blood lactate dehydrogenase increased			

subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Cardiac murmur			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Troponin increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Weight increased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
White blood cell count increased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Fall			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	0	2
Contusion			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Procedural pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	2
Radius fracture			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Rib fracture			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Skin abrasion			

subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Acute myocardial infarction			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Atrial fibrillation			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Coronary artery disease			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Nervous system disorders			
Headache			
subjects affected / exposed	2 / 17 (11.76%)	1 / 8 (12.50%)	4 / 12 (33.33%)
occurrences (all)	2	1	5
Dizziness			
subjects affected / exposed	1 / 17 (5.88%)	1 / 8 (12.50%)	3 / 12 (25.00%)
occurrences (all)	1	1	3
Dysgeusia			
subjects affected / exposed	2 / 17 (11.76%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	2	0	1
Tremor			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Paraesthesia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Peripheral sensory neuropathy			

subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Neuropathy peripheral			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Akathisia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Cognitive disorder			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Diabetic neuropathy			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Haemorrhage intracranial			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	2
Hypoaesthesia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Peripheral motor neuropathy			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Polyneuropathy			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Sciatica			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Taste disorder			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Visual field defect			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			

Neutropenia			
subjects affected / exposed	1 / 17 (5.88%)	1 / 8 (12.50%)	4 / 12 (33.33%)
occurrences (all)	1	7	15
Lymphopenia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Leukopenia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 8 (12.50%)	1 / 12 (8.33%)
occurrences (all)	0	7	4
Anaemia			
subjects affected / exposed	0 / 17 (0.00%)	2 / 8 (25.00%)	2 / 12 (16.67%)
occurrences (all)	0	3	5
Thrombocytopenia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 8 (12.50%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Autoimmune haemolytic anaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	2
Ear and labyrinth disorders			
Ear discomfort			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Eye disorder			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Eye pruritus			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	3 / 17 (17.65%)	2 / 8 (25.00%)	5 / 12 (41.67%)
occurrences (all)	5	4	8
Nausea			
subjects affected / exposed	2 / 17 (11.76%)	0 / 8 (0.00%)	4 / 12 (33.33%)
occurrences (all)	3	0	4
Vomiting			

subjects affected / exposed	4 / 17 (23.53%)	0 / 8 (0.00%)	3 / 12 (25.00%)
occurrences (all)	4	0	4
Abdominal pain			
subjects affected / exposed	1 / 17 (5.88%)	1 / 8 (12.50%)	2 / 12 (16.67%)
occurrences (all)	1	1	3
Constipation			
subjects affected / exposed	2 / 17 (11.76%)	1 / 8 (12.50%)	1 / 12 (8.33%)
occurrences (all)	2	2	1
Dyspepsia			
subjects affected / exposed	2 / 17 (11.76%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	2	0	4
Haemorrhoids			
subjects affected / exposed	0 / 17 (0.00%)	1 / 8 (12.50%)	1 / 12 (8.33%)
occurrences (all)	0	1	1
Abdominal pain upper			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Abdominal pain lower			
subjects affected / exposed	0 / 17 (0.00%)	1 / 8 (12.50%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Flatulence			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Proctalgia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Stomatitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Toothache			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Dysphagia			

subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Hepatobiliary disorders			
Hepatocellular injury			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Night sweats			
subjects affected / exposed	2 / 17 (11.76%)	1 / 8 (12.50%)	3 / 12 (25.00%)
occurrences (all)	2	1	3
Pruritus			
subjects affected / exposed	2 / 17 (11.76%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	2	0	2
Rash maculo-papular			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	0	7
Rash			
subjects affected / exposed	1 / 17 (5.88%)	1 / 8 (12.50%)	2 / 12 (16.67%)
occurrences (all)	1	1	2
Dry skin			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Erythema			
subjects affected / exposed	0 / 17 (0.00%)	1 / 8 (12.50%)	0 / 12 (0.00%)
occurrences (all)	0	2	0
Exfoliative rash			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Hyperhidrosis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Hyperkeratosis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Lividity			

subjects affected / exposed	0 / 17 (0.00%)	1 / 8 (12.50%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Onychomadesis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Rash pruritic			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Skin lesion			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Skin mass			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Urinary incontinence			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Urinary retention			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 17 (11.76%)	0 / 8 (0.00%)	3 / 12 (25.00%)
occurrences (all)	2	0	5
Bone pain			
subjects affected / exposed	3 / 17 (17.65%)	0 / 8 (0.00%)	2 / 12 (16.67%)
occurrences (all)	6	0	2
Muscular weakness			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	3 / 12 (25.00%)
occurrences (all)	1	0	5
Muscle spasms			

subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	2 / 12 (16.67%)
occurrences (all)	1	0	2
Myalgia			
subjects affected / exposed	2 / 17 (11.76%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	3	0	1
Osteoarthritis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	0	2
Pain in extremity			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	0	2
Flank pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Musculoskeletal chest pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	0	2
Neck pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Amyotrophy			
subjects affected / exposed	0 / 17 (0.00%)	1 / 8 (12.50%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Iliolumbar syndrome			
subjects affected / exposed	0 / 17 (0.00%)	1 / 8 (12.50%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Joint swelling			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Back pain			
subjects affected / exposed	0 / 17 (0.00%)	1 / 8 (12.50%)	0 / 12 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			

Urinary tract infection			
subjects affected / exposed	3 / 17 (17.65%)	1 / 8 (12.50%)	0 / 12 (0.00%)
occurrences (all)	4	1	0
Bronchitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	2 / 12 (16.67%)
occurrences (all)	1	0	2
Pneumonia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Nasopharyngitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Sinusitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	2 / 12 (16.67%)
occurrences (all)	1	0	2
Upper respiratory tract infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	2
Oral candidiasis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Rhinitis			
subjects affected / exposed	1 / 17 (5.88%)	1 / 8 (12.50%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
Conjunctivitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0
Furuncle			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Laryngitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Sinusitis aspergillus			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1

Skin infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Tooth abscess			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Tracheobronchitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Influenza			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	5 / 17 (29.41%)	1 / 8 (12.50%)	1 / 12 (8.33%)
occurrences (all)	5	1	1
Hyperkalaemia			
subjects affected / exposed	1 / 17 (5.88%)	1 / 8 (12.50%)	2 / 12 (16.67%)
occurrences (all)	1	3	4
Hypokalaemia			
subjects affected / exposed	2 / 17 (11.76%)	0 / 8 (0.00%)	2 / 12 (16.67%)
occurrences (all)	3	0	2
Hyperglycaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hypomagnesaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Hypoalbuminaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0
Hyponatraemia			
subjects affected / exposed	2 / 17 (11.76%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	2	0	0
Dehydration			

subjects affected / exposed	1 / 17 (5.88%)	1 / 8 (12.50%)	0 / 12 (0.00%)
occurrences (all)	1	1	0
Hypophosphataemia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Hyperuricaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	2
Hypoglycaemia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	1	0	1
Hypernatraemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 8 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	0	1
Iron deficiency			
subjects affected / exposed	1 / 17 (5.88%)	0 / 8 (0.00%)	0 / 12 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Part 2/3: Cohort A	Part 2/3: Cohort B	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	32 / 33 (96.97%)	29 / 30 (96.67%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant muscle neoplasm			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Seborrhoeic keratosis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Tumour pain			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 33 (9.09%)	2 / 30 (6.67%)	
occurrences (all)	6	4	
Flushing			

subjects affected / exposed	1 / 33 (3.03%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Hot flush			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Hypotension			
subjects affected / exposed	1 / 33 (3.03%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Lymphostasis			
subjects affected / exposed	0 / 33 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	2	
Cyanosis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Deep vein thrombosis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Peripheral arterial occlusive disease			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Phlebitis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	7 / 33 (21.21%)	2 / 30 (6.67%)	
occurrences (all)	13	3	
Pyrexia			
subjects affected / exposed	6 / 33 (18.18%)	4 / 30 (13.33%)	
occurrences (all)	9	4	
Asthenia			
subjects affected / exposed	0 / 33 (0.00%)	5 / 30 (16.67%)	
occurrences (all)	0	6	
Oedema peripheral			

subjects affected / exposed	0 / 33 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	2	
Chills			
subjects affected / exposed	1 / 33 (3.03%)	2 / 30 (6.67%)	
occurrences (all)	1	2	
Non-cardiac chest pain			
subjects affected / exposed	1 / 33 (3.03%)	1 / 30 (3.33%)	
occurrences (all)	1	1	
Hyperthermia			
subjects affected / exposed	0 / 33 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	4	
Pain			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Chest pain			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Facial pain			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Swelling			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Reproductive system and breast disorders			
Breast pain			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 33 (9.09%)	2 / 30 (6.67%)	
occurrences (all)	3	6	
Dyspnoea			
subjects affected / exposed	1 / 33 (3.03%)	4 / 30 (13.33%)	
occurrences (all)	4	4	
Nasal congestion			

subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Oropharyngeal pain			
subjects affected / exposed	0 / 33 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Pleural effusion			
subjects affected / exposed	0 / 33 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Rhinorrhoea			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Hypoxia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Pharyngeal erythema			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Productive cough			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Pulmonary mass			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Stridor			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	2 / 33 (6.06%)	2 / 30 (6.67%)	
occurrences (all)	4	4	
Anxiety			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Confusional state			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	

Investigations			
Neutrophil count decreased			
subjects affected / exposed	2 / 33 (6.06%)	2 / 30 (6.67%)	
occurrences (all)	3	5	
Lymphocyte count decreased			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
White blood cell count decreased			
subjects affected / exposed	1 / 33 (3.03%)	3 / 30 (10.00%)	
occurrences (all)	1	3	
Platelet count decreased			
subjects affected / exposed	0 / 33 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	4	
Alanine aminotransferase increased			
subjects affected / exposed	1 / 33 (3.03%)	1 / 30 (3.33%)	
occurrences (all)	1	1	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 33 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 33 (3.03%)	1 / 30 (3.33%)	
occurrences (all)	1	1	
Weight decreased			
subjects affected / exposed	1 / 33 (3.03%)	1 / 30 (3.33%)	
occurrences (all)	1	2	
Blood creatinine increased			
subjects affected / exposed	1 / 33 (3.03%)	1 / 30 (3.33%)	
occurrences (all)	1	1	
Gamma-glutamyltransferase increased			
subjects affected / exposed	2 / 33 (6.06%)	1 / 30 (3.33%)	
occurrences (all)	2	1	
Blood bilirubin increased			
subjects affected / exposed	1 / 33 (3.03%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Body temperature increased			

subjects affected / exposed	1 / 33 (3.03%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Haemoglobin decreased			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Cardiac murmur			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Troponin increased			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Weight increased			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
White blood cell count increased			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	2 / 33 (6.06%)	2 / 30 (6.67%)	
occurrences (all)	3	2	
Fall			
subjects affected / exposed	1 / 33 (3.03%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Contusion			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Procedural pain			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Radius fracture			

subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Rib fracture			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Skin abrasion			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	2 / 33 (6.06%)	0 / 30 (0.00%)	
occurrences (all)	2	0	
Tachycardia			
subjects affected / exposed	0 / 33 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Acute myocardial infarction			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Atrial fibrillation			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Coronary artery disease			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 33 (3.03%)	1 / 30 (3.33%)	
occurrences (all)	1	3	
Dizziness			
subjects affected / exposed	0 / 33 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Dysgeusia			
subjects affected / exposed	1 / 33 (3.03%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Tremor			

subjects affected / exposed	1 / 33 (3.03%)	2 / 30 (6.67%)	
occurrences (all)	1	2	
Paraesthesia			
subjects affected / exposed	1 / 33 (3.03%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 33 (3.03%)	1 / 30 (3.33%)	
occurrences (all)	1	1	
Neuropathy peripheral			
subjects affected / exposed	1 / 33 (3.03%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Akathisia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Cognitive disorder			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Diabetic neuropathy			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Haemorrhage intracranial			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Hypoaesthesia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Peripheral motor neuropathy			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Polyneuropathy			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Sciatica			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Taste disorder			

subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Visual field defect			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	21 / 33 (63.64%)	17 / 30 (56.67%)	
occurrences (all)	48	52	
Lymphopenia			
subjects affected / exposed	8 / 33 (24.24%)	6 / 30 (20.00%)	
occurrences (all)	16	32	
Leukopenia			
subjects affected / exposed	5 / 33 (15.15%)	7 / 30 (23.33%)	
occurrences (all)	9	23	
Anaemia			
subjects affected / exposed	7 / 33 (21.21%)	5 / 30 (16.67%)	
occurrences (all)	10	7	
Thrombocytopenia			
subjects affected / exposed	4 / 33 (12.12%)	6 / 30 (20.00%)	
occurrences (all)	5	9	
Autoimmune haemolytic anaemia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Ear and labyrinth disorders			
Ear discomfort			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Eye disorders			
Eye disorder			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Eye pruritus			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			

Diarrhoea			
subjects affected / exposed	5 / 33 (15.15%)	2 / 30 (6.67%)	
occurrences (all)	5	3	
Nausea			
subjects affected / exposed	2 / 33 (6.06%)	4 / 30 (13.33%)	
occurrences (all)	2	6	
Vomiting			
subjects affected / exposed	1 / 33 (3.03%)	3 / 30 (10.00%)	
occurrences (all)	1	3	
Abdominal pain			
subjects affected / exposed	0 / 33 (0.00%)	6 / 30 (20.00%)	
occurrences (all)	0	6	
Constipation			
subjects affected / exposed	1 / 33 (3.03%)	2 / 30 (6.67%)	
occurrences (all)	2	3	
Dyspepsia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Haemorrhoids			
subjects affected / exposed	2 / 33 (6.06%)	1 / 30 (3.33%)	
occurrences (all)	2	1	
Abdominal pain upper			
subjects affected / exposed	1 / 33 (3.03%)	3 / 30 (10.00%)	
occurrences (all)	1	3	
Abdominal pain lower			
subjects affected / exposed	0 / 33 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	2	
Flatulence			
subjects affected / exposed	0 / 33 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Proctalgia			
subjects affected / exposed	1 / 33 (3.03%)	0 / 30 (0.00%)	
occurrences (all)	2	0	

Stomatitis			
subjects affected / exposed	0 / 33 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Toothache			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Dysphagia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Hepatobiliary disorders			
Hepatocellular injury			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
Night sweats			
subjects affected / exposed	2 / 33 (6.06%)	0 / 30 (0.00%)	
occurrences (all)	2	0	
Pruritus			
subjects affected / exposed	2 / 33 (6.06%)	1 / 30 (3.33%)	
occurrences (all)	3	1	
Rash maculo-papular			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Rash			
subjects affected / exposed	0 / 33 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Dry skin			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Erythema			
subjects affected / exposed	1 / 33 (3.03%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Exfoliative rash			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Hyperhidrosis			

subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Hyperkeratosis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Lividity			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Onychomadesis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Rash pruritic			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Skin lesion			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Skin mass			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Urinary incontinence			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Urinary retention			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 33 (9.09%)	1 / 30 (3.33%)	
occurrences (all)	4	8	
Bone pain			

subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Muscular weakness			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Muscle spasms			
subjects affected / exposed	2 / 33 (6.06%)	0 / 30 (0.00%)	
occurrences (all)	2	0	
Myalgia			
subjects affected / exposed	1 / 33 (3.03%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Osteoarthritis			
subjects affected / exposed	1 / 33 (3.03%)	0 / 30 (0.00%)	
occurrences (all)	3	0	
Pain in extremity			
subjects affected / exposed	1 / 33 (3.03%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Flank pain			
subjects affected / exposed	1 / 33 (3.03%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Neck pain			
subjects affected / exposed	0 / 33 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Amyotrophy			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Iliolumbar syndrome			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Joint swelling			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal pain			

subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Back pain			
subjects affected / exposed	1 / 33 (3.03%)	2 / 30 (6.67%)	
occurrences (all)	1	3	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	3 / 33 (9.09%)	1 / 30 (3.33%)	
occurrences (all)	5	1	
Bronchitis			
subjects affected / exposed	4 / 33 (12.12%)	1 / 30 (3.33%)	
occurrences (all)	5	1	
Pneumonia			
subjects affected / exposed	0 / 33 (0.00%)	3 / 30 (10.00%)	
occurrences (all)	0	6	
Nasopharyngitis			
subjects affected / exposed	1 / 33 (3.03%)	1 / 30 (3.33%)	
occurrences (all)	2	1	
Sinusitis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 33 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	2	
Oral candidiasis			
subjects affected / exposed	1 / 33 (3.03%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Rhinitis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Conjunctivitis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Furuncle			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	

Laryngitis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Sinusitis aspergillus			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Skin infection			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Tooth abscess			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Tracheobronchitis			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Influenza			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 33 (3.03%)	3 / 30 (10.00%)	
occurrences (all)	1	6	
Hyperkalaemia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Hypokalaemia			
subjects affected / exposed	0 / 33 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	3	
Hyperglycaemia			
subjects affected / exposed	2 / 33 (6.06%)	1 / 30 (3.33%)	
occurrences (all)	4	2	
Hypomagnesaemia			
subjects affected / exposed	1 / 33 (3.03%)	0 / 30 (0.00%)	
occurrences (all)	5	0	
Hypoalbuminaemia			

subjects affected / exposed	2 / 33 (6.06%)	2 / 30 (6.67%)	
occurrences (all)	2	3	
Hyponatraemia			
subjects affected / exposed	0 / 33 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	3	
Dehydration			
subjects affected / exposed	0 / 33 (0.00%)	1 / 30 (3.33%)	
occurrences (all)	0	1	
Hypophosphataemia			
subjects affected / exposed	1 / 33 (3.03%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Hyperuricaemia			
subjects affected / exposed	1 / 33 (3.03%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Hypoglycaemia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Hypernatraemia			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	
Iron deficiency			
subjects affected / exposed	0 / 33 (0.00%)	0 / 30 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 February 2016	a) Revisions and editing for consistency and clarity b) The exploratory objectives were expanded to include gene expression profiling and genomic analysis of relevant genes, and the corresponding endpoint was revised accordingly c) Inclusion and exclusion criteria and schedule of events were revised d) Toxicity management guidelines were revised to improve consistency and define dose-modifying events e) The guidelines for subject discontinuation and collection of subsequent anti-cancer therapy were revised f) The hematology and serum chemistry assessments and description of record retention were streamlined g) The Ann Arbor staging criteria (with cotswold modifications) were added to the protocol.
23 June 2017	a) Administrative changes related to the transfer of the compound from ImmunoGen Inc. to Debiopharm International S.A. b) Cohorts 1 and 2 were specified.
23 February 2018	a) Part 2 and Part 3 were introduced with the subject population restricted to r/r DLBCL who had responded to the last prior DLBCL systemic therapy and had achieved a duration of response (CR or PR) of at least 8 weeks (from the last day of the last cycle). Primary refractory subjects were excluded. The change was aimed at having a more homogeneous population for data analysis. b) A new once every week (QW) Debio 1562 dosing schedule (Cohort B) was added while maintaining the Q3W Debio 1562 dosing arm (Cohort A), without increasing the cumulative Debio 1562 dose currently allowed in the protocol (i.e., 0.7 mg/kg – 1.0 mg/kg Q3W). c) Cohort 1 (enrolling DLBCL with a huge proportion of primary refractory and refractory to last line subjects) and Cohort 2 (enrolling other NHL subjects) were stopped. d) The fixed study design was changed to an adaptive design to utilize the generated data to establish a dosing regimen associated with optimal benefit-risk. e) Blood sampling time points were added to improve evaluation of PK disposition f) Pharmacodynamic and drug metabolism enzymes and transporters (DMET) assessments were added g) Health-related quality of life (HRQoL) assessment was added.
19 December 2018	a) The eligibility criteria were updated to exclude subjects presenting interstitial lung disease, diffuse parenchymal lung disease, or with a past history of severe/Grade 3 parenchymal lung disorder b) The monitoring period was extended to 4 h after completion of the rituximab infusion for the first cycle c) A new section of risk minimization measures for the expected serious adverse reactions was introduced.

23 February 2020	a) The main reason for this amendment was to exceptionally allow treatment prolongation beyond 6 cycles, provided the subject is benefitting from the study drug. b) The following changes associated with treatment prolongation were added: imaging modality of radiologic tumor response assessments, timepoint of the last PK, immunogenicity, immunophenotyping, and HRQoL assessments c) Clarification that primary analysis will be conducted after all enrolled subject reach their 3rd on-treatment scheduled response assessment or they discontinue treatment, and that the final analysis will be triggered one year after the last accrued subject's first dose date. Clarification that the data from treatment prolongation will be summarized in an addendum. d) Clarification that the potential immunogenicity against rituximab will be assessed.
24 April 2020	This amendment was following an urgent safety measure during the COVID-19 pandemic to reduce risks to subjects visiting study sites. The main modification was to allow subjects on the QW Debio 1562 dosing regimen to switch to the Q3W dosing regimen to reduce the frequency of their visits to hospitals. This also entailed the addition of a sensitivity analysis for subjects who switched their treatment regimen.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported