Clinical trial results:
A Two-arm, Phase 1b/2 Study of IPI-145 Administered in Combination with Rituximab or Obinutuzumab in Subjects with Previously Untreated CD20+ Follicular Lymphoma

Summary

EudraCT number	2014-005459-13
Trial protocol	IT BE ES GB
Global end of trial date	06 January 2017

Results information

Result version number	v2 (current)
This version publication date	25 November 2023
First version publication date	06 July 2018
Version creation reason	• Correction of full data set Results contact has changed.
Summary attachment (see zip file)	Sponsor Statement (2. Sponsor statement.pdf) Transferring letter from Infinity (3. Transferring letter from Infinity.pdf) Transferring letter from Verastem (4. Transferring letter from Verastem.pdf)

Trial information

Trial identification

Sponsor protocol code	IPI-145-19

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	IND Number: 112,486

Notes:

Sponsors

Sponsor organisation name	Secura Bio, Inc.
Sponsor organisation address	1995 Village Center Circle, Suite 128, Las Vegas, NV, United States, 89134
Public contact	Beth Gregory, PharmD, MBA , Secura Bio, Inc., 1 702-254-0011, bgregory@securabio.com
Scientific contact	Beth Gregory, PharmD, MBA , Secura Bio, Inc., 1 702-254-0011, bgregory@securabio.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	No

1901/2006 apply to this trial?	

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	27 December 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	06 January 2017
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Evaluate the safety and assess the clinical activityof IPI-145 in combination with rituximab or obinutuzumab in subjects with previously untreated CD20+ follicular lymphoma (FL)

Protection of trial subjects:

Prior to screening for enrollment into the clinical trial, all patients were provided detailed information about the investigational product and the trial. During the informed consent process, patients were allowed to ask questions and have a conversation with the study staff providing consent. The informed consent form (ICF) included all elements required by ICH, GCP, and adhered to the IRB/IEC requirements and the ethical principles that have their origin in the Declaration of Helsinki. It was explained to patients during this conversation that they have the right to withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. The ICF was updated when important new information became available, and all patients still receiving treatment in the trial were re-consented on the new information.
During the trial, protection of trial subjects took the form of adverse event and concomitant medication monitoring, and disease response monitoring. Adverse events (AEs) were monitored from the time of signing the ICF. The Protocol provided information on what concomitant medication and therapies were either not allowed or should be used with caution. An assessment of these medications and therapies was performed at every clinic visit. Lastly, disease response assessments were performed according to the schedule stipulated in the Protocol. If a study subject progressed, appropriate conversations were had with their study investigator to determine the best course of action for further treatment or management of their disease, outside of the clinical trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 May 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 13
Country: Number of subjects enrolled	United Kingdom: 5
Country: Number of subjects enrolled	United States: 19
Country: Number of subjects enrolled	Belgium: 9
Country: Number of subjects enrolled	France: 7
Country: Number of subjects enrolled	Italy: 2

Worldwide total number of subjects	55
EEA total number of subjects	36

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)	36
From 65 to 84 years	19
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

The Screening Period Assessments will occur over a period of up to 30 days prior to first dose of study drug (Cycle 1 Day 1).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Duvelisib (25 mg BID) + Rituximab

Arm description:

Subjects self-administered duvelisib orally continuously twice per day (BID) over 28-day treatment cycles. Rituximab was administered as an intravenous (IV) infusion (375 mg/m) in four weekly doses in an Induction Period and then a dose was administered every 2 cycles (12 doses) in the Maintenance Period for a total of up to 16 doses.

Arm type	Experimental
Investigational medicinal product name	Duvelisib
Investigational medicinal product code	IPI-145
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Duvelisib will be self-administered BID at a starting dose of 25 mg (or, if determined by DLT assessment, a lower dose of 15 mg) in 28-day cycles beginning on the morning of Cycle 1 Day 1.

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:

Rituximab will be administered by IV infusion at a dose of 375 mg/m2. A treatment cycle is defined as lasting 28 days.

Arm title	Duvelisib (25 mg BID) + Obinutuzumab

Arm description:

Subjects self-administered duvelisib orally continuously BID over 28-day treatment cycles. Obinutuzumab was administered as an IV infusion (1000 mg) in four weekly doses in the Induction Period and then a dose was administered every 2 cycles (12 doses) in the Maintenance Period for a total of up to 16 doses.

Arm type	Experimental
Investigational medicinal product name	Duvelisib
Investigational medicinal product code	IPI-145
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details: Duvelisib will be self-administered BID at a starting dose of 25 mg (or, if determined by DLT assessment, a lower dose of 15 mg) in 28-day cycles beginning on the morning of Cycle 1 Day 1.	
Investigational medicinal product name	Obinutuzumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Obinutuzumab will be administered by IV infusion at a dose of 1000 mg. A treatment cycle is defined as lasting 28 days.

Number of subjects in period 1	Duvelisib (25 mg BID) + Rituximab	Duvelisib (25 mg BID) + Obinutuzumab
Started	28	27
Completed	0	1
Not completed	28	26
Consent withdrawn by subject	1	-
Death	2	-
Other	4	6
Termination of the study by the sponsor	20	20
Lost to follow-up	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Duvelisib (25 mg BID) + Rituximab
Reporting group description:	
Subjects self-administered duvelisib orally continuously twice per day (BID) over 28-day treatment cycles. Rituximab was administered as an intravenous (IV) infusion (375 mg/m) in four weekly doses in an Induction Period and then a dose was administered every 2 cycles (12 doses) in the Maintenance Period for a total of up to 16 doses.	
Reporting group title	Duvelisib (25 mg BID) + Obinutuzumab
Reporting group description:	
Subjects self-administered duvelisib orally continuously BID over 28-day treatment cycles. Obinutuzumab was administered as an IV infusion (1000 mg) in four weekly doses in the Induction Period and then a dose was administered every 2 cycles (12 doses) in the Maintenance Period for a total of up to 16 doses.	

Reporting group values	Duvelisib (25 mg BID) + Rituximab	Duvelisib (25 mg BID) + Obinutuzumab	Total
Number of subjects	28	27	55
Age categorical Units: Subjects			
Adults (18-64 years)	20	16	36
From 65-84 years	8	11	19
Age continuous Units: years			
arithmetic mean	58.2	58.4	
full range (min-max)	36 to 79	32 to 77	-
Gender categorical Units: Subjects			
Female	10	16	26
Male	18	11	29

End points

End points reporting groups

Reporting group title	Duvelisib (25 mg BID) + Rituximab

Reporting group description:

Subjects self-administered duvelisib orally continuously twice per day (BID) over 28-day treatment cycles. Rituximab was administered as an intravenous (IV) infusion (375 mg/m) in four weekly doses in an Induction Period and then a dose was administered every 2 cycles (12 doses) in the Maintenance Period for a total of up to 16 doses.

Reporting group title	Duvelisib (25 mg BID) + Obinutuzumab

Reporting group description:

Subjects self-administered duvelisib orally continuously BID over 28-day treatment cycles. Obinutuzumab was administered as an IV infusion (1000 mg) in four weekly doses in the Induction Period and then a dose was administered every 2 cycles (12 doses) in the Maintenance Period for a total of up to 16 doses.

Primary: Dose Limiting Toxicities

End point title	Dose Limiting Toxicities[1]

End point description:

The dose limiting toxicity (DLT)-Evaluable analysis set was defined as all subjects in Part 1 of the study who either experienced a DLT during Cycle 1 or completed at least 75% of the prescribed Cycle 1 doses of duvelisib and rituximab or duvelisib and obinutuzumab. This analysis set was used to determine the dose level for Part 2.

One DLT occurred in the DO arm: Grade 3 elevated lipase on Day 8 of study treatment. Treatment with duvelisib was interrupted and obinutuzumab was continued.

End point type	Primary

End point timeframe:

All subjects in Part 1 of the study who either experienced a DLT during Cycle 1 or completed at least 75% of the prescribed Cycle 1 doses of duvelisib and rituximab or duvelisib and obinutuzumab.

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: Data were summarized as descriptive statistics only for this endpoint.

End point values	Duvelisib (25 mg BID) + Rituximab	Duvelisib (25 mg BID) + Obinutuzumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6[2]		
Units: Number of subjects	0	1		

Notes:

[2] - 1 DLT in DO arm: Treatment with duvelisib was interrupted and obinutuzumab was continued.

Statistical analyses

No statistical analyses for this end point

Primary: Complete Response (CR)

End point title	Complete Response (CR)[3]

End point description:

CRR was tested against the null (≤ 15%) by a 1-sided exact binomial test at 0.05 level for each arm separately. The estimated CRR along with the 2-sided 95% exact confidence interval was provided. Subjects with missing data for overall response was assumed as not having achieved a CR.

In the DR arm, 10 (35.7%) subjects had a best response of Complete Response (CR).
In the DO arm, 11 (40.7%) subjects had a best response of Complete Response (CR).

End point type	Primary

End point timeframe:

Throughout the study

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: Data were summarized as descriptive statistics only for this endpoint.

End point values	Duvelisib (25 mg BID) + Rituximab	Duvelisib (25 mg BID) + Obinutuzumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	27		
Units: Number of subjects	10	11		

Statistical analyses

No statistical analyses for this end point

Secondary: Anemia - Maximum Post-Baseline Grade

End point title	Anemia - Maximum Post-Baseline Grade

End point description:

Completed when result different from 0 for at least one arm

End point type	Secondary

End point timeframe:

Throughout the study

End point values	Duvelisib (25 mg BID) + Rituximab	Duvelisib (25 mg BID) + Obinutuzumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	27		
Units: Number of subjects				
Baseline value 0 / Max end value 0	13	11		
Baseline value 0 / Max end value 1	6	11		
Baseline value 1 / Max end value 0	3	0		
Baseline value 1 / Max end value 1	4	2		
Baseline value 1 / Max end value 2	1	1		
Baseline value 2 / Max end value 1	1	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Hemoglobin increased -Maximum Post-Baseline Grade

End point title	Hemoglobin increased -Maximum Post-Baseline Grade
End point description: Completed when result different from 0 for at least one arm	
End point type	Secondary
End point timeframe: Throughout the study	

End point values	Duvelisib (25 mg BID) + Rituximab	Duvelisib (25 mg BID) + Obinutuzumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	27		
Units: Number of subjects				
Baseline value 0/Max end value 0	28	27		

Statistical analyses

No statistical analyses for this end point

Secondary: Leukocytosis - Maximum Post-Baseline Grade

End point title	Leukocytosis - Maximum Post-Baseline Grade
End point description: Completed when result different from 0 for at least one arm	
End point type	Secondary
End point timeframe: Throughout the study	

End point values	Duvelisib (25 mg BID) + Rituximab	Duvelisib (25 mg BID) + Obinutuzumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	27		
Units: Number of subjects				
Baseline value 0/Max end value 0	28	27		

Statistical analyses

No statistical analyses for this end point

Secondary: Lymphocyte count decreased - Maximum Post-Baseline Grade

End point title	Lymphocyte count decreased - Maximum Post-Baseline Grade

End point description:

Completed when result different from 0 for at least one arm

End point type	Secondary

End point timeframe:

Throughout the study

End point values	Duvelisib (25 mg BID) + Rituximab	Duvelisib (25 mg BID) + Obinutuzumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	27		
Units: Number of subjects				
Baseline value 0 / Max end value 0	10	3		
Baseline value 0 / Max end value 1	5	3		
Baseline value 0 / Max end value 2	0	9		
Baseline value 0 / Max end value 3	1	2		
Baseline value 0 / Max end value 4	0	1		
Baseline value 1 / Max end value 0	2	0		
Baseline value 1 / Max end value 1	4	3		
Baseline value 1 / Max end value 2	2	1		
Baseline value 1 / Max end value 4	0	1		
Baseline value 2 / Max end value 0	1	0		
Baseline value 2 / Max end value 2	2	2		
Baseline value 2 / Max end value 3	1	1		
Baseline value 3 / Max end value 3	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Lymphocyte count increased - Maximum Post-Baseline Grade

End point title	Lymphocyte count increased - Maximum Post-Baseline Grade
End point description:	
Completed when result different from 0 for at least one arm	
End point type	Secondary
End point timeframe:	
Throughout the study	

End point values	Duvelisib (25 mg BID) + Rituximab	Duvelisib (25 mg BID) + Obinutuzumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	27		
Units: Number of subjects				
Baseline value 0 / Max end value 0	23	21		
Baseline value 0 / Max end value 2	4	4		
Baseline value 0 / Max end value 3	0	1		
Baseline value 2 / Max end value 0	0	1		
Baseline value 2 / Max end value 2	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Neutrophil count decreased - Maximum Post-Baseline Grade

End point title	Neutrophil count decreased - Maximum Post-Baseline Grade
End point description:	
Completed when result different from 0 for at least one arm	
End point type	Secondary
End point timeframe:	
Throughout the study	

End point values	Duvelisib (25 mg BID) + Rituximab	Duvelisib (25 mg BID) + Obinutuzumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	24		
Units: Number of subjects				
Baseline value 0 / Max end value 0	5	3		
Baseline value 0 / Max end value 1	10	8		
Baseline value 0 / Max end value 2	2	0		
Baseline value 0 / Max end value 3	1	2		
Baseline value 0 / Max end value 4	1	3		
Baseline value 1 / Max end value 1	1	2		
Baseline value 1 / Max end value 2	2	1		
Baseline value 1 / Max end value 3	3	4		

Baseline value 1 / Max end value 4	1	0		
Baseline value 2 / Max end value 3	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Platelet count decreased - Maximum Post-Baseline Grade

End point title	Platelet count decreased - Maximum Post-Baseline Grade
End point description:	
Completed when result different from 0 for at least one arm	
End point type	Secondary
End point timeframe:	
Throughout the study	

End point values	Duvelisib (25 mg BID) + Rituximab	Duvelisib (25 mg BID) + Obinutuzumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	27		
Units: Number of subjects				
Baseline value 0 / Max end value 0	21	13		
Baseline value 0 / Max end value 1	3	9		
Baseline value 0 / Max end value 2	0	1		
Baseline value 0 / Max end value 3	1	0		
Baseline value 1 / Max end value 0	1	1		
Baseline value 1 / Max end value 1	2	3		

Statistical analyses

No statistical analyses for this end point

Secondary: White blood cell decreased - Maximum Post-Baseline Grade

End point title	White blood cell decreased - Maximum Post-Baseline Grade
End point description:	
Completed when result different from 0 for at least one arm	
End point type	Secondary
End point timeframe:	
Throughout the study	

End point values	Duvelisib (25 mg BID) + Rituximab	Duvelisib (25 mg BID) + Obinutuzumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	27		
Units: Number of subjects				
Baseline value 0 / Max end value 0	12	9		
Baseline value 0 / Max end value 1	11	10		
Baseline value 0 / Max end value 2	1	3		
Baseline value 1 / Max end value 1	2	1		
Baseline value 1 / Max end value 2	1	2		
Baseline value 1 / Max end value 3	0	1		
Baseline value 2 / Max end value 2	1	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Creatinine increased - Maximum Post-Baseline Grade

End point title	Creatinine increased - Maximum Post-Baseline Grade
End point description:	
Completed when result different from 0 for at least one arm	
End point type	Secondary
End point timeframe:	
Throughout the study	

End point values	Duvelisib (25 mg BID) + Rituximab	Duvelisib (25 mg BID) + Obinutuzumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	27		
Units: Number of subjects				
Baseline value 0/Max end value 0	27	26		
Baseline value 0/Max end value 1	0	1		
Baseline value 1 / Max end value 0	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Hypercalcemia - Maximum Post-Baseline Grade

End point title	Hypercalcemia - Maximum Post-Baseline Grade
End point description:	
Completed when result different from 0 for at least one arm	
End point type	Secondary

End point timeframe:
Throughout the study

End point values	Duvelisib (25 mg BID) + Rituximab	Duvelisib (25 mg BID) + Obinutuzumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	27		
Units: Number of subjects				
Baseline value 0/Max end value 0	28	27		

Statistical analyses

No statistical analyses for this end point

Secondary: Hyperkalemia-Maximum post -Baseline grade

End point title	Hyperkalemia-Maximum post -Baseline grade

End point description:
Completed when result different from 0 for at least one arm

End point type	Secondary

End point timeframe:
Throughout the study

End point values	Duvelisib (25 mg BID) + Rituximab	Duvelisib (25 mg BID) + Obinutuzumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	27		
Units: Number of subjects				
Baseline value 0/Max end value 0	22	24		
Baseline value 0/Max end value 1	4	1		
Baseline value 0 / Max end value 2	1	0		
Baseline value 0 / Max end value 4	0	1		
Baseline value 1 / Max end value 0	0	1		
Baseline value 2 / Max end value 2	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Hypermagnesemia - Maximum post -Baseline grade

End point title	Hypermagnesemia - Maximum post -Baseline grade

End point description:	
Completed when result different from 0 for at least one arm	
End point type	Secondary
End point timeframe:	
Throughout the study	

End point values	Duvelisib (25 mg BID) + Rituximab	Duvelisib (25 mg BID) + Obinutuzumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	24		
Units: Number of subjects				
Baseline value 0/Max end value 0	23	24		
Baseline value 0 / Max end value 3	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Hypernatremia - Maximum post -Baseline grade

End point title	Hypernatremia - Maximum post -Baseline grade
End point description:	
Completed when result different from 0 for at least one arm	
End point type	Secondary
End point timeframe:	
Throughout the study	

End point values	Duvelisib (25 mg BID) + Rituximab	Duvelisib (25 mg BID) + Obinutuzumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	27		
Units: Number of subjects				
Baseline value 0/Max end value 0	25	23		
Baseline value 0/Max end value 1	3	2		
Baseline value 0 / Max end value 2	0	1		
Baseline value 1 / Max end value 0	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Hypoalbuminemia - Maximum post -Baseline grade

End point title	Hypoalbuminemia - Maximum post -Baseline grade

End point description:

Completed when result different from 0 for at least one arm

End point type	Secondary

End point timeframe:

Throughout the study

End point values	Duvelisib (25 mg BID) + Rituximab	Duvelisib (25 mg BID) + Obinutuzumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	26		
Units: Number of subjects				
Baseline value 0/Max end value 0	23	16		
Baseline value 0/Max end value 1	4	7		
Baseline value 0 / Max end value 2	0	1		
Baseline value 1 / Max end value 0	0	1		
Baseline value 1 / Max end value 2	0	1		
Baseline value 2 / Max end value 2	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Hypocalcemia - Maximum post -Baseline grade

End point title	Hypocalcemia - Maximum post -Baseline grade

End point description:

Completed when result different from 0 for at least one arm

End point type	Secondary

End point timeframe:

Throughout the study

End point values	Duvelisib (25 mg BID) + Rituximab	Duvelisib (25 mg BID) + Obinutuzumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	27		
Units: Number of subjects				
Baseline value 0/Max end value 0	20	10		
Baseline value 0 / Max end value 1	5	13		
Baseline value 1 / Max end value 0	0	1		
Baseline value 1 / Max end value 1	3	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Hypoglycemia - Maximum post -Baseline grade

End point title	Hypoglycemia - Maximum post -Baseline grade

End point description:

Completed when result different from 0 for at least one arm

End point type	Secondary

End point timeframe:

Throughout the study

End point values	Duvelisib (25 mg BID) + Rituximab	Duvelisib (25 mg BID) + Obinutuzumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	27		
Units: Number of subjects				
Baseline value 0/Max end value 0	21	16		
Baseline value 0 / Max end value 1	4	9		
Baseline value 1 / Max end value 0	0	1		
Baseline value 1 / Max end value 1	2	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Hypokalemia - Maximum post -Baseline grade

End point title	Hypokalemia - Maximum post -Baseline grade

End point description:

Completed when result different from 0 for at least one arm

End point type	Secondary

End point timeframe:

Throughout the study

End point values	Duvelisib (25 mg BID) + Rituximab	Duvelisib (25 mg BID) + Obinutuzumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	27		
Units: Number of subjects				
Baseline value 0/Max end value 0	25	21		
Baseline value 0 / Max end value 1	3	4		
Baseline value 0 / Max end value 3	0	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Hypomagnesemia- Maximum post -Baseline grade

End point title	Hypomagnesemia- Maximum post -Baseline grade

End point description:

Completed when result different from 0 for at least one arm

End point type	Secondary

End point timeframe:

Throughout the study

End point values	Duvelisib (25 mg BID) + Rituximab	Duvelisib (25 mg BID) + Obinutuzumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	24		
Units: Number of subjects				
Baseline value 0/Max end value 0	15	10		
Baseline value 0 / Max end value 1	5	8		
Baseline value 0 / Max end value 3	0	1		
Baseline value 1 / Max end value 1	4	5		

Statistical analyses

No statistical analyses for this end point

Secondary: Hyponatremia - Maximum post -Baseline grade

End point title	Hyponatremia - Maximum post -Baseline grade

End point description:

Completed when result different from 0 for at least one arm

End point type	Secondary

End point timeframe:

Throughout the study

End point values	Duvelisib (25 mg BID) + Rituximab	Duvelisib (25 mg BID) + Obinutuzumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	27		
Units: Number of subjects				
Baseline value 0/Max end value 0	19	23		
Baseline value 0/Max end value 1	9	3		
Baseline value 1/ Max end value 1	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Hypophosphatemia - Maximum post -Baseline grade

End point title	Hypophosphatemia - Maximum post -Baseline grade
End point description:	
Completed when result different from 0 for at least one arm	
End point type	Secondary
End point timeframe:	
Throughout the study	

End point values	Duvelisib (25 mg BID) + Rituximab	Duvelisib (25 mg BID) + Obinutuzumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	24	25		
Units: Number of subjects				
Baseline value 0 / Max end value 0	10	5		
Baseline value 0 / Max end value 1	10	7		
Baseline value 0 / Max end value 2	1	4		
Baseline value 0 / Max end value 3	0	2		
Baseline value 1 / Max end value 1	1	5		
Baseline value 1 / Max end value 2	2	1		
Baseline value 2 / Max end value 2	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Lipase increased - Maximum post -Baseline grade

End point title	Lipase increased - Maximum post -Baseline grade

End point description:

Completed when result different from 0 for at least one arm

End point type	Secondary

End point timeframe:

Throughout the study

End point values	Duvelisib (25 mg BID) + Rituximab	Duvelisib (25 mg BID) + Obinutuzumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	20		
Units: Number of subjects				
Baseline value 0/Max end value 0	17	16		
Baseline value 0 / Max end value 1	4	1		
Baseline value 0 / Max end value 3	2	1		
Baseline value 0 / Max end value 4	0	1		
Baseline value 1 / Max end value 2	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Serum amylase increased - Maximum post -Baseline grade

End point title	Serum amylase increased - Maximum post -Baseline grade

End point description:

Completed when result different from 0 for at least one arm

End point type	Secondary

End point timeframe:

Throughout the study

End point values	Duvelisib (25 mg BID) + Rituximab	Duvelisib (25 mg BID) + Obinutuzumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	23		
Units: Number of subjects				
Baseline value 0/Max end value 0	21	21		
Baseline value 0 / Max end value 1	1	1		
Baseline value 0 / Max end value 3	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Alanine aminotransferase increased- Maximum post -Baseline grade

End point title	Alanine aminotransferase increased- Maximum post -Baseline grade

End point description:

Completed when result different from 0 for at least one arm

End point type	Secondary

End point timeframe:

Throughout the study

End point values	Duvelisib (25 mg BID) + Rituximab	Duvelisib (25 mg BID) + Obinutuzumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	27		
Units: Number of subjects				
Baseline value 0 / Max end value 0	0	5		
Baseline value 0 / Max end value 1	12	9		
Baseline value 0 / Max end value 2	2	4		
Baseline value 0 / Max end value 3	6	4		
Baseline value 0 / Max end value 4	2	3		
Baseline value 1 / Max end value 0	1	0		
Baseline value 1 / Max end value 1	2	0		
Baseline value 1 / Max end value 3	3	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Alkaline phosphatase increased- Maximum Post-Baseline Grade

End point title	Alkaline phosphatase increased- Maximum Post-Baseline Grade

End point description:

Completed when result different from 0 for at least one arm

End point type	Secondary

End point timeframe:

Throughout the study

End point values	Duvelisib (25 mg BID) + Rituximab	Duvelisib (25 mg BID) + Obinutuzumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	27		
Units: Number of subjects				
Baseline value 0 / Max end value 0	18	21		
Baseline value 0 / Max end value 1	5	3		
Baseline value 0 / Max end value 2	0	1		
Baseline value 0 / Max end value 3	0	1		
Baseline value 1 / Max end value 0	3	0		
Baseline value 1 / Max end value 1	2	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Aspartate aminotransferase increased- Maximum post -Baseline grade

End point title	Aspartate aminotransferase increased- Maximum post - Baseline grade

End point description:

Completed when result different from 0 for at least one arm

End point type	Secondary

End point timeframe:

Throughout the study

End point values	Duvelisib (25 mg BID) + Rituximab	Duvelisib (25 mg BID) + Obinutuzumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	24		
Units: Number of subjects				
Baseline value 0 / Max end value 0	4	7		
Baseline value 0 / Max end value 1	9	8		
Baseline value 0 / Max end value 2	4	3		
Baseline value 0 / Max end value 3	2	5		
Baseline value 0 / Max end value 4	1	0		
Baseline value 1 / Max end value 0	3	0		
Baseline value 1 / Max end value 1	3	0		
Baseline value 1 / Max end value 3	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Blood bilirubin increased - Maximum Post-Baseline Grade

End point title	Blood bilirubin increased - Maximum Post-Baseline Grade

End point description:

Completed when result different from 0 for at least one arm

End point type	Secondary

End point timeframe:

Throughout the study

End point values	Duvelisib (25 mg BID) + Rituximab	Duvelisib (25 mg BID) + Obinutuzumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	27		
Units: Number of subjects				
Baseline value 0 / Max end value 0	20	18		
Baseline value 0 / Max end value 1	6	6		
Baseline value 0 / Max end value 2	1	1		
Baseline value 1 / Max end value 0	0	1		
Baseline value 1 / Max end value 1	1	0		
Baseline value 2 / Max end value 3	0	1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

For all subjects (including screen-failures), monitoring of AEs will be performed from the signing of the ICF through 30 days after the last dose or until the subject is deemed a study failure.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups

Reporting group title	Duvelisib (25 mg BID) + Rituximab
Reporting group description: -	
Reporting group title	Duvelisib (25 mg BID) + Obinutuzumab

Reporting group description: -

Serious adverse events	Duvelisib (25 mg BID) + Rituximab	Duvelisib (25 mg BID) + Obinutuzumab	
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 28 (35.71%)	16 / 27 (59.26%)	
number of deaths (all causes)	2	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lymphoma			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of skin			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Embolism			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			

Pyrexia			
subjects affected / exposed	2 / 28 (7.14%)	4 / 27 (14.81%)	
occurrences causally related to treatment / all	0 / 2	2 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mucosal inflammation			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 28 (3.57%)	1 / 27 (3.70%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 28 (0.00%)	2 / 27 (7.41%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Infusion related reaction			

subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	1 / 28 (3.57%)	2 / 27 (7.41%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	4 / 28 (14.29%)	2 / 27 (7.41%)	
occurrences causally related to treatment / all	4 / 4	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Odynophagia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stomatitis			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Vomiting			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatotoxicity			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 28 (3.57%)	2 / 27 (7.41%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash papular			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash generalised			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (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			
Renal failure			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Conjunctivitis			

subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea infectious			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Klebsiella infection			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia respiratory syncytial viral			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus infection			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumocystis jirovecii infection			

subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia cytomegaloviral			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Pneumonia pneumococcal			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Duvelisib (25 mg BID) + Rituximab	Duvelisib (25 mg BID) + Obinutuzumab	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 28 (96.43%)	26 / 27 (96.30%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Uterine leiomyoma			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Lymphoma			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Squamous cell carcinoma of skin			

subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			
Flushing			
subjects affected / exposed	1 / 28 (3.57%)	1 / 27 (3.70%)	
occurrences (all)	1	1	
Hypotension			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Orthostatic hypotension			
subjects affected / exposed	2 / 28 (7.14%)	1 / 27 (3.70%)	
occurrences (all)	2	1	
Embolism			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Hypertension			
subjects affected / exposed	3 / 28 (10.71%)	0 / 27 (0.00%)	
occurrences (all)	3	0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	6 / 28 (21.43%)	10 / 27 (37.04%)	
occurrences (all)	6	10	
Fatigue			
subjects affected / exposed	9 / 28 (32.14%)	8 / 27 (29.63%)	
occurrences (all)	9	8	
Asthenia			
subjects affected / exposed	5 / 28 (17.86%)	4 / 27 (14.81%)	
occurrences (all)	5	4	
Malaise			
subjects affected / exposed	1 / 28 (3.57%)	4 / 27 (14.81%)	
occurrences (all)	1	4	
Mucosal inflammation			
subjects affected / exposed	3 / 28 (10.71%)	2 / 27 (7.41%)	
occurrences (all)	3	2	
Chills			

subjects affected / exposed	2 / 28 (7.14%)	1 / 27 (3.70%)	
occurrences (all)	2	1	
Discomfort			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Oedema peripheral			
subjects affected / exposed	1 / 28 (3.57%)	1 / 27 (3.70%)	
occurrences (all)	1	1	
Peripheral swelling			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Systematic inflammatory response syndrome			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Chest discomfort			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Localised oedema			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Pain			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	0 / 28 (0.00%)	2 / 27 (7.41%)	
occurrences (all)	0	2	
Hypersensitivity			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
Breast discomfort			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Erectile dysfunction			

subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Oedema genital			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Penile erythema			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	7 / 28 (25.00%)	6 / 27 (22.22%)	
occurrences (all)	7	6	
Oropharyngeal pain			
subjects affected / exposed	2 / 28 (7.14%)	4 / 27 (14.81%)	
occurrences (all)	2	4	
Dyspnoea			
subjects affected / exposed	4 / 28 (14.29%)	3 / 27 (11.11%)	
occurrences (all)	4	3	
Pneumonitis			
subjects affected / exposed	1 / 28 (3.57%)	2 / 27 (7.41%)	
occurrences (all)	1	2	
Rhinorrhoea			
subjects affected / exposed	0 / 28 (0.00%)	2 / 27 (7.41%)	
occurrences (all)	0	2	
Dyspnoea exertional			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Nasal congestion			
subjects affected / exposed	1 / 28 (3.57%)	1 / 27 (3.70%)	
occurrences (all)	1	1	
Paranasal sinus discomfort			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Productive cough			

subjects affected / exposed	2 / 28 (7.14%)	1 / 27 (3.70%)	
occurrences (all)	2	1	
Sinus congestion			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Throat irritation			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Wheezing			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	5 / 28 (17.86%)	3 / 27 (11.11%)	
occurrences (all)	5	3	
Depression			
subjects affected / exposed	1 / 28 (3.57%)	2 / 27 (7.41%)	
occurrences (all)	1	2	
Insomnia			
subjects affected / exposed	2 / 28 (7.14%)	1 / 27 (3.70%)	
occurrences (all)	2	1	
Libido decreased			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	9 / 28 (32.14%)	14 / 27 (51.85%)	
occurrences (all)	9	14	
Aspartate aminotransferase increased			
subjects affected / exposed	8 / 28 (28.57%)	13 / 27 (48.15%)	
occurrences (all)	8	13	
Amylase increased			
subjects affected / exposed	3 / 28 (10.71%)	3 / 27 (11.11%)	
occurrences (all)	3	3	
Lipase increased			

subjects affected / exposed	3 / 28 (10.71%)	3 / 27 (11.11%)	
occurrences (all)	3	3	
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Blood magnesium decreased			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Eosinophil count increased			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Liver function test abnormal			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Neutrophil count decreased			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Transaminases increased			
subjects affected / exposed	3 / 28 (10.71%)	1 / 27 (3.70%)	
occurrences (all)	3	1	
Weight decreased			
subjects affected / exposed	1 / 28 (3.57%)	1 / 27 (3.70%)	
occurrences (all)	1	1	
Weight increased			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	1 / 28 (3.57%)	4 / 27 (14.81%)	
occurrences (all)	1	4	
Excoriation			

subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Skin abrasion			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Procedural pain			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Tongue injury			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Wound			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Sinus tachycardia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Atrial fibrillation			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Supraventricular tachycardia			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	1 / 28 (3.57%)	4 / 27 (14.81%)	
occurrences (all)	1	4	
Headache			
subjects affected / exposed	4 / 28 (14.29%)	4 / 27 (14.81%)	
occurrences (all)	4	4	
Dizziness			
subjects affected / exposed	1 / 28 (3.57%)	2 / 27 (7.41%)	
occurrences (all)	1	2	
Paraesthesia			

subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Sedation			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Hemiparesis			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Syncope			
subjects affected / exposed	1 / 28 (3.57%)	1 / 27 (3.70%)	
occurrences (all)	1	1	
Tremor			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Dysaesthesia			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Hypoaesthesia			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Polyneuropathy			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	4 / 28 (14.29%)	5 / 27 (18.52%)	
occurrences (all)	4	5	
Anaemia			
subjects affected / exposed	2 / 28 (7.14%)	1 / 27 (3.70%)	
occurrences (all)	2	1	
Febrile neutropenia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	

Leukocytosis			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Thrombocytopenia			
subjects affected / exposed	2 / 28 (7.14%)	1 / 27 (3.70%)	
occurrences (all)	2	1	
Leukopenia			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 28 (0.00%)	2 / 27 (7.41%)	
occurrences (all)	0	2	
Ear pain			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Ear pruritus			
subjects affected / exposed	1 / 28 (3.57%)	1 / 27 (3.70%)	
occurrences (all)	1	1	
Eye disorders			
Eye pain			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Eyelid oedema			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Periorbital oedema			
subjects affected / exposed	1 / 28 (3.57%)	1 / 27 (3.70%)	
occurrences (all)	1	1	
Vision blurred			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Visual acuity reduced			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			

Nausea			
subjects affected / exposed	7 / 28 (25.00%)	12 / 27 (44.44%)	
occurrences (all)	7	12	
Diarrhoea			
subjects affected / exposed	16 / 28 (57.14%)	11 / 27 (40.74%)	
occurrences (all)	16	11	
Abdominal pain			
subjects affected / exposed	5 / 28 (17.86%)	8 / 27 (29.63%)	
occurrences (all)	5	8	
Vomiting			
subjects affected / exposed	4 / 28 (14.29%)	8 / 27 (29.63%)	
occurrences (all)	4	8	
Abdominal pain upper			
subjects affected / exposed	2 / 28 (7.14%)	5 / 27 (18.52%)	
occurrences (all)	2	5	
Constipation			
subjects affected / exposed	5 / 28 (17.86%)	4 / 27 (14.81%)	
occurrences (all)	5	4	
Stomatitis			
subjects affected / exposed	1 / 28 (3.57%)	4 / 27 (14.81%)	
occurrences (all)	1	4	
Gastrooesophageal reflux disease			
subjects affected / exposed	3 / 28 (10.71%)	3 / 27 (11.11%)	
occurrences (all)	3	3	
Colitis			
subjects affected / exposed	2 / 28 (7.14%)	2 / 27 (7.41%)	
occurrences (all)	2	2	
Dyspepsia			
subjects affected / exposed	0 / 28 (0.00%)	2 / 27 (7.41%)	
occurrences (all)	0	2	
Odynophagia			
subjects affected / exposed	1 / 28 (3.57%)	2 / 27 (7.41%)	
occurrences (all)	1	2	
Toothache			
subjects affected / exposed	0 / 28 (0.00%)	2 / 27 (7.41%)	
occurrences (all)	0	2	

Abdominal discomfort			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Diverticulum			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Dry mouth			
subjects affected / exposed	1 / 28 (3.57%)	1 / 27 (3.70%)	
occurrences (all)	1	1	
Functional gastrointestinal disorder			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Gastrointestinal hypermotility			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Gingival bleeding			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Oesophagitis			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Oral mucosal erythema			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Proctitis			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Abdominal pain lower			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Aphthous ulcer			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Mouth ulceration			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	

Oral pain			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Proctalgia			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Hepatobiliary disorders			
Cholestasis			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Hepatotoxicity			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Hepatitis			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	8 / 28 (28.57%)	8 / 27 (29.63%)	
occurrences (all)	8	8	
Dry skin			
subjects affected / exposed	2 / 28 (7.14%)	3 / 27 (11.11%)	
occurrences (all)	2	3	
Alopecia			
subjects affected / exposed	1 / 28 (3.57%)	2 / 27 (7.41%)	
occurrences (all)	1	2	
Rash erythematous			
subjects affected / exposed	1 / 28 (3.57%)	2 / 27 (7.41%)	
occurrences (all)	1	2	
Eczema asteatotic			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Erythema			
subjects affected / exposed	2 / 28 (7.14%)	1 / 27 (3.70%)	
occurrences (all)	2	1	
Hyperhidrosis			

subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Night sweats			
subjects affected / exposed	1 / 28 (3.57%)	1 / 27 (3.70%)	
occurrences (all)	1	1	
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Pigmentation disorder			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Pruritus			
subjects affected / exposed	3 / 28 (10.71%)	1 / 27 (3.70%)	
occurrences (all)	3	1	
Psoriasis			
subjects affected / exposed	1 / 28 (3.57%)	1 / 27 (3.70%)	
occurrences (all)	1	1	
Purpura			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Rash maculo-papular			
subjects affected / exposed	1 / 28 (3.57%)	1 / 27 (3.70%)	
occurrences (all)	1	1	
Rash papular			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Skin exfoliation			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Dermatitis			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Eczema			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	

Erythema multiforme			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Exfoliative rash			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Hand dermatitis			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Rash generalised			
subjects affected / exposed	2 / 28 (7.14%)	0 / 27 (0.00%)	
occurrences (all)	2	0	
Skin hypopigmentation			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Skin lesion			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Dysuria			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Renal failure			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Pollakiuria			
subjects affected / exposed	2 / 28 (7.14%)	0 / 27 (0.00%)	
occurrences (all)	2	0	
Endocrine disorders			
Cushingoid			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			

Back pain			
subjects affected / exposed	6 / 28 (21.43%)	3 / 27 (11.11%)	
occurrences (all)	6	3	
Arthralgia			
subjects affected / exposed	1 / 28 (3.57%)	2 / 27 (7.41%)	
occurrences (all)	1	2	
Muscle spasms			
subjects affected / exposed	0 / 28 (0.00%)	2 / 27 (7.41%)	
occurrences (all)	0	2	
Arthritis			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Musculoskeletal pain			
subjects affected / exposed	1 / 28 (3.57%)	1 / 27 (3.70%)	
occurrences (all)	1	1	
Pain in extremity			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Limb discomfort			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Muscular weakness			
subjects affected / exposed	2 / 28 (7.14%)	0 / 27 (0.00%)	
occurrences (all)	2	0	
Musculoskeletal discomfort			
subjects affected / exposed	2 / 28 (7.14%)	0 / 27 (0.00%)	
occurrences (all)	2	0	
Myalgia			
subjects affected / exposed	3 / 28 (10.71%)	0 / 27 (0.00%)	
occurrences (all)	3	0	
Infections and infestations			
Nasopharyngitis			

subjects affected / exposed	1 / 28 (3.57%)	6 / 27 (22.22%)	
occurrences (all)	1	6	
Conjunctivitis			
subjects affected / exposed	1 / 28 (3.57%)	4 / 27 (14.81%)	
occurrences (all)	1	4	
Sinusitis			
subjects affected / exposed	1 / 28 (3.57%)	2 / 27 (7.41%)	
occurrences (all)	1	2	
Upper respiratory tract infection			
subjects affected / exposed	2 / 28 (7.14%)	2 / 27 (7.41%)	
occurrences (all)	2	2	
Angular cheilitis			
subjects affected / exposed	1 / 28 (3.57%)	1 / 27 (3.70%)	
occurrences (all)	1	1	
Bacterial diarrhoea			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Bronchitis			
subjects affected / exposed	1 / 28 (3.57%)	1 / 27 (3.70%)	
occurrences (all)	1	1	
Candida infections			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Cystitis			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Dermatitis infected			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Diarrhoea infectious			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Folliculitis			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Genital herpes simplex			

subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Herpes virus infection			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Herpes zoster			
subjects affected / exposed	1 / 28 (3.57%)	1 / 27 (3.70%)	
occurrences (all)	1	1	
Klebsiella infection			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Labyrinthitis			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Oral herpes			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Otitis media			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Pneumonia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Pneumonia respiratory syncytial viral			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Pyelonephritis			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Respiratory tract infection			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Rhinitis			
subjects affected / exposed	1 / 28 (3.57%)	1 / 27 (3.70%)	
occurrences (all)	1	1	
Sepsis			

subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Septic shock			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Tinea infection			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Urinary tract infection			
subjects affected / exposed	1 / 28 (3.57%)	1 / 27 (3.70%)	
occurrences (all)	1	1	
Urinary tract infection bacterial			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Anal abscess			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Campylobacter gastroenteritis			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Corona virus infection			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Cytomegalovirus infection			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Gastroenteritis			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Hordeolum			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Laryngitis			

subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Lung infection			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Pneumocystis jirovecii infection			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Pneumonia cytomegaloviral			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Pneumonia pneumococcal			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Staphylococcal infection			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Tinea cruris			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 28 (3.57%)	6 / 27 (22.22%)	
occurrences (all)	1	6	
Hypokalaemia			
subjects affected / exposed	1 / 28 (3.57%)	3 / 27 (11.11%)	
occurrences (all)	1	3	
Hypomagnesaemia			
subjects affected / exposed	0 / 28 (0.00%)	2 / 27 (7.41%)	
occurrences (all)	0	2	
Hypophosphataemia			
subjects affected / exposed	0 / 28 (0.00%)	2 / 27 (7.41%)	
occurrences (all)	0	2	

Hypoalbuminaemia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Hypocalcaemia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Hypoglycaemia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Tumour lysis syndrome			
subjects affected / exposed	0 / 28 (0.00%)	1 / 27 (3.70%)	
occurrences (all)	0	1	
Gout			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	
Hyperkalaemia			
subjects affected / exposed	1 / 28 (3.57%)	0 / 27 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 February 2015	Amendment 1, Global
22 October 2015	Amendment 2, Global
19 September 2016	Amendment 3, Global. Amendment 3 was not submitted in the EU but was submitted in US but never implemented. No subjects were enrolled under Amendment 3.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
16 June 2016	On the 16th June an Administrative Letter requesting an enrollment hold in Europe until Amendment 3 was approved was issued to all EU investigators.	-

Notes:

Limitations and caveats

None reported