Clinical trial results:
A Phase 1/2 Study on the Safety of Rovalpituzumab Tesirine Administered in Combination with Nivolumab or Nivolumab and Ipilimumab for Adults with Extensive-Stage Small Cell Lung Cancer.

Summary

EudraCT number	2016-003686-26
Trial protocol	DE ES IT
Global end of trial date	03 July 2019

Results information

Result version number	v2 (current)
This version publication date	17 July 2020
First version publication date	15 May 2020
Version creation reason	• New data added to full data set Editorial change to clarify age ranges and an outcome measure description.

Trial information

Trial identification

Sponsor protocol code	M16-300

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03026166
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Abbvie Deutschland GmbH & Co.KG
Sponsor organisation address	AbbVie House, Vanwall Business Park, Maidenhead, Berkshire, United Kingdom, SL6-4UB
Public contact	Global Medical Services, AbbVie, 011 800-633-9110,
Scientific contact	Philip Komarnitsky, MD, PhD, AbbVie, philip.komarnitsky@abbvie.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	03 July 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 July 2019
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to assess the safety of rovalpituzumab tesirine when administered in combination with nivolumab or nivolumab and ipilimumab in adult subjects with extensive-stage small cell lung cancer (SCLC).

Protection of trial subjects:

All subjects entering the study had to sign an informed consent that was explained to them and questions encouraged.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 March 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 10
Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Italy: 3
Country: Number of subjects enrolled	United States: 28
Worldwide total number of subjects	42
EEA total number of subjects	14

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)	26
From 65 to 84 years	16

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at 17 clinical study sites in 4 countries: United States, France, Italy, and Germany.

Pre-assignment

Screening details:

Three study cohorts were planned to enroll approximately 30 subjects in each, including a dose-limiting toxicity (DLT) evaluation phase (the first 12 weeks of any treatment for all subjects) and an expansion phase. However, Cohort 2 was limited to 12 subjects and Cohort 3 was not opened.

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	Cohort 1: Rovalpituzumab Tesirine and Nivolumab

Arm description:

Participants received 2 doses of 0.3 mg/kg rovalpituzumab tesirine by intravenous (IV) infusion 6 weeks apart (Day 1 of Cycles 1 and 3), and 2 doses of 360 mg nivolumab IV 3 weeks apart beginning on Cycle 2 (Day 1 of Cycles 2 and 3).
Participants then received maintenance therapy with 480 mg nivolumab IV once every 4 weeks from Cycle 4 until disease progression.

Arm type	Experimental
Investigational medicinal product name	Rovalpituzumab Tesirine)
Investigational medicinal product code	SC16LD6.5
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered by intravenous infusion 0.3 mg/kg, every 6 weeks (q6wk) × 2

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

Dosage and administration details:

Administered by intravenous infusion

Arm title	Cohort 2: Rovalpituzumab Tesirine and Nivolumab + Ipilimumab

Arm description:

Participants received 2 doses of 0.3 mg/kg rovalpituzumab tesirine IV 6 weeks apart (Day 1 of Cycles 1 and 3), nivolumab 1 mg/kg every 3 weeks for 4 cycles beginning on Cycle 2 (Day 1 of Cycles 2-5), and ipilimumab 1 mg/kg IV every 3 weeks for 4 cycles beginning on Cycle 2 (Day 1 of Cycles 2-5).
After a 6-week washout, participants then received maintenance therapy with 480 mg nivolumab IV once every 4 weeks from Cycle 6 until disease progression.

Arm type	Experimental

Investigational medicinal product name	Rovalpituzumab Tesirine
Investigational medicinal product code	SC16LD6.5
Other name	
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Administered by intravenous infusion 0.3 mg/kg, every 6 weeks (q6wk) × 2

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

Dosage and administration details:

Administered by intravenous infusion

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

Dosage and administration details:

Administered by intravenous infusion 1 mg/kg once every 3 weeks

Number of subjects in period 1	Cohort 1: Rovalpituzumab Tesirine and Nivolumab	Cohort 2: Rovalpituzumab Tesirine and Nivolumab + Ipilimumab
Started	30	12
Completed	0	0
Not completed	30	12
Physician decision	2	-
Consent withdrawn by subject	1	2
Death	22	7
Other	1	-
Study Terminated by Sponsor	3	3
Lost to follow-up	1	-

Baseline characteristics

Reporting groups

Reporting group title	Cohort 1: Rovalpituzumab Tesirine and Nivolumab

Reporting group description:

Participants received 2 doses of 0.3 mg/kg rovalpituzumab tesirine by intravenous (IV) infusion 6 weeks apart (Day 1 of Cycles 1 and 3), and 2 doses of 360 mg nivolumab IV 3 weeks apart beginning on Cycle 2 (Day 1 of Cycles 2 and 3).
Participants then received maintenance therapy with 480 mg nivolumab IV once every 4 weeks from Cycle 4 until disease progression.

Reporting group title	Cohort 2: Rovalpituzumab Tesirine and Nivolumab + Ipilimumab

Reporting group description:

Participants received 2 doses of 0.3 mg/kg rovalpituzumab tesirine IV 6 weeks apart (Day 1 of Cycles 1 and 3), nivolumab 1 mg/kg every 3 weeks for 4 cycles beginning on Cycle 2 (Day 1 of Cycles 2-5), and ipilimumab 1 mg/kg IV every 3 weeks for 4 cycles beginning on Cycle 2 (Day 1 of Cycles 2-5).
After a 6-week washout, participants then received maintenance therapy with 480 mg nivolumab IV once every 4 weeks from Cycle 6 until disease progression.

Reporting group values	Cohort 1: Rovalpituzumab Tesirine and Nivolumab	Cohort 2: Rovalpituzumab Tesirine and Nivolumab + Ipilimumab	Total
Number of subjects	30	12	42
Age categorical Units: Subjects			
< 40 years	0	1	1
≥ 40 to < 60 years	11	5	16
≥ 60 years	19	6	25
Age continuous Units: years			
arithmetic mean	61.87	57.25	
standard deviation	± 8.195	± 14.085	-
Gender categorical Units: Subjects			
Female	14	5	19
Male	16	7	23
Race Units: Subjects			
White	29	10	39
Black or African American	1	1	2
Not Reported	0	1	1
Ethnicity Units: Subjects			
Hispanic or Latino	2	0	2
Not Hispanic or Latino	28	11	39
Not Reported	0	1	1

End points

End points reporting groups

Reporting group title	Cohort 1: Rovalpituzumab Tesirine and Nivolumab

Reporting group description:

Participants received 2 doses of 0.3 mg/kg rovalpituzumab tesirine by intravenous (IV) infusion 6 weeks apart (Day 1 of Cycles 1 and 3), and 2 doses of 360 mg nivolumab IV 3 weeks apart beginning on Cycle 2 (Day 1 of Cycles 2 and 3).
Participants then received maintenance therapy with 480 mg nivolumab IV once every 4 weeks from Cycle 4 until disease progression.

Reporting group title	Cohort 2: Rovalpituzumab Tesirine and Nivolumab + Ipilimumab

Reporting group description:

Participants received 2 doses of 0.3 mg/kg rovalpituzumab tesirine IV 6 weeks apart (Day 1 of Cycles 1 and 3), nivolumab 1 mg/kg every 3 weeks for 4 cycles beginning on Cycle 2 (Day 1 of Cycles 2-5), and ipilimumab 1 mg/kg IV every 3 weeks for 4 cycles beginning on Cycle 2 (Day 1 of Cycles 2-5).
After a 6-week washout, participants then received maintenance therapy with 480 mg nivolumab IV once every 4 weeks from Cycle 6 until disease progression.

Primary: Number of Participants with Dose-limiting Toxicities (DLTs)

End point title	Number of Participants with Dose-limiting Toxicities (DLTs)[1]

End point description:

Dose-limiting toxicities were defined as any of the following in the 12-week DLT-evaluation period, graded according to the National Cancer Institute's Common Terminology Criteria for Adverse Events (NCI CTCAE), version 4.03:
● Grade 4 thrombocytopenia (or Grade 3 thrombocytopenia with bleeding) lasting more than 7 days and/or requiring platelet transfusion
● Grade 4 neutropenia lasting more than 7 days, and/or requiring hematopoietic growth factor rescue, or any febrile neutropenia (Grade 3 or 4 neutropenia with concurrent fever ≥ 38.3°C)
● Grade 4 anemia unrelated to underlying disease
● Clinically significant Grade 3 or 4 non-hematologic laboratory abnormality that did not resolve to Grade 0/1 or baseline within 7 days
● Grade 3 or 4 non-laboratory adverse event (AE), except fatigue, asthenia, nausea, or other manageable constitutional symptom
DLT-evaluable participants were those who completed 4 cycles treatment during the DLT period or stopped treatment earlier due to DLT.

End point type	Primary

End point timeframe:

12 weeks

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: Comparisons between cohorts were not conducted.

End point values	Cohort 1: Rovalpituzumab Tesirine and Nivolumab	Cohort 2: Rovalpituzumab Tesirine and Nivolumab + Ipilimumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6[2]	6[3]		
Units: participants	1	3		

Notes:

[2] - DLT-evaluable

[3] - DLT evaluable

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Adverse Events (AEs)

End point title	Number of Participants with Adverse Events (AEs)[4]

End point description:

The investigator rated the severity of each AE according to the NCI CTCAE Version 4.03 and according to the following:
Grade 1: The AE is transient and easily tolerated by the subject (mild).
Grade 2: The AE causes the subject discomfort and interrupts the subject's usual activities (moderate).
Grade 3/4: The AE causes considerable interference with the subject's usual activities and may be incapacitating or life-threatening (severe).
Grade 5: The AE resulted in death of the subject (severe).
The maximum severity of AEs are reported.

A serious adverse event was defined as an AE meeting any of the following:
- Death
- Life-threatening
- Resulted in hospitalization or prolongation of hospitalization
- Resulted in congenital abnormality
- Resulted in persistent or significant disability or incapacity
- Was an important medical event requiring medical intervention to prevent a serious outcome.
Relationship to study drug was assessed by the Investigator.

End point type	Primary

End point timeframe:

From the first dose of study drug until 100 days after the last dose of study drug; median duration of treatment was 65 days and 53 days in each cohort respectively.

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: Comparisons between cohorts were not conducted.

End point values	Cohort 1: Rovalpituzumab Tesirine and Nivolumab	Cohort 2: Rovalpituzumab Tesirine and Nivolumab + Ipilimumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	12		
Units: participants				
Any adverse event	30	12		
Drug-related adverse event	29	12		
Serious adverse event	23	9		
Drug-related serious adverse event	13	6		
Grade 3 adverse event	11	7		
Grade 4 adverse event	1	1		
Grade 5 adverse event	14	4		
Drug-related Grade 3 adverse event	9	10		

Drug-related Grade 4 adverse event	3	1		
Drug-related Grade 5 adverse event	4	0		
AE leading to study drug withdrawal	12	6		
AE leading to treatment interruption	18	8		
AE leading to dose reduction	0	1		
Drug-related AE leading to study drug withdrawal	9	4		
Drug-related AE leading to treatment interruption	17	8		
Drug-related AE leading to dose reduction	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate

End point title	Objective Response Rate

End point description:

Treatment response was assessed by radiographic tumor evaluations conducted by a central radiology review.
Objective response rate (ORR) is defined as the percentage of participants whose best overall response is either a confirmed complete response (CR) or partial response (PR) according to Response Evaluation Criteria for Solid Tumors (RECIST) v1.1.
Complete response (CR): Disappearance of all target lesions. Any pathological lymph nodes must have reduction in short axis to < 10 mm.
Partial response (PR): A ≥ 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters.
CR or PR must have been confirmed at least 4 weeks (28 days) from the initial determination per RECIST v 1.1.
The Efficacy Analysis Set includes participants who received at least one dose of study drug, had a target lesion identified at baseline, and either had at least 1 post-dose tumor assessment or discontinued treatment due to AE, progressive disease (PD) or death.

End point type	Secondary

End point timeframe:

Cohort 1: at Week 6, Week 13, and every 8 weeks thereafter; Cohort 2: at Week 6, Week 12, Week 18, and every 8 weeks thereafter, up to the end of follow-up; median duration on follow-up was 31.7 and 48.0 weeks in each cohort respectively.

End point values	Cohort 1: Rovalpituzumab Tesirine and Nivolumab	Cohort 2: Rovalpituzumab Tesirine and Nivolumab + Ipilimumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29[5]	11[6]		
Units: percentage of participants				
number (confidence interval 95%)	27.6 (12.7 to 47.2)	36.4 (10.9 to 69.2)		

Notes:

[5] - Efficacy Analysis Set

[6] - Efficacy Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response

End point title	Duration of Response

End point description:

Duration of overall response is defined as the time from the date of first documented CR or PR, assessed by central radiology review and based on RECIST v. 1.1, to the documented date of progressive disease (PD) or death, whichever occurred first. Participants who neither progressed nor died were censored at the last evaluable disease assessment. Based on Kaplan-Meier estimate.
Progressive disease was defined as at least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study, with an absolute increase of at least 0.5 cm, or the unequivocal progression of non-target lesions, or the appearance of one or more new lesions.
The analysis includes participants in the Efficacy Analysis Set with a best overall response of unconfirmed CR or PR.
"99999" indicates a value that could not be estimated.

End point type	Secondary

End point timeframe:

Cohort 1: at Week 6, Week 13, and every 8 weeks thereafter; Cohort 2: at Week 6, Week 12, Week 18 and every 8 weeks thereafter, up to the end of follow-up; median duration on follow-up was 31.7 and 48.0 weeks in each cohort respectively.

End point values	Cohort 1: Rovalpituzumab Tesirine and Nivolumab	Cohort 2: Rovalpituzumab Tesirine and Nivolumab + Ipilimumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10[7]	6[8]		
Units: months				
median (confidence interval 95%)	3.8 (1.6 to 5.6)	3.3 (1.4 to 99999)		

Notes:

[7] - Efficacy analysis set participants with unconfirmed CR or PR

[8] - Efficacy analysis set participants with unconfirmed CR or PR

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival

End point title	Progression-Free Survival

End point description:

Progression-free survival is defined as the time from the first dose date to the documented date of PD or death, whichever occurred first, based on central radiology review according to RECIST v 1.1. Participants who neither progressed nor died were censored at the last evaluable disease assessment. Based on Kaplan-Meier estimates.
Progressive disease was defined as at least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study, with an absolute increase of at least 0.5 cm, or the unequivocal progression of non-target lesions, or the appearance of one or more new lesions.
Efficacy Analysis Set.

End point type	Secondary

End point timeframe:

From first dose of study drug up to the end of follow-up; median duration on follow-up was 31.7 and 48.0 weeks in each cohort respectively.

End point values	Cohort 1: Rovalpituzumab Tesirine and Nivolumab	Cohort 2: Rovalpituzumab Tesirine and Nivolumab + Ipilimumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29[9]	11[10]		
Units: months				
median (confidence interval 95%)	4.8 (3.2 to 5.3)	4.1 (1.3 to 6.0)		

Notes:

[9] - Efficacy Analysis Set

[10] - Efficacy Analysis Set

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

End point title	Overall Survival

End point description:

Overall survival is defined as the time from the first dose date to death for any reason. Participants who were still alive were censored at the last known alive date. Based on Kaplan-Meier estimates.
The Full Analysis Set includes participants who received at least one dose of study drug.

End point type	Secondary

End point timeframe:

From first dose of study drug up to the end of follow-up; median duration on follow-up was 31.7 and 48.0 weeks in each cohort respectively.

End point values	Cohort 1: Rovalpituzumab Tesirine and Nivolumab	Cohort 2: Rovalpituzumab Tesirine and Nivolumab + Ipilimumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30[11]	12[12]		
Units: months				
median (confidence interval 95%)	7.4 (5.0 to 9.1)	11.0 (2.3 to 17.0)		

Notes:

[11] - Full analysis set

[12] - Full analysis set

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the first dose of study drug until 100 days after the last dose of study drug; median duration of treatment was 65 days and 53 days in each cohort respectively.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups

Reporting group title	Cohort 2: Rovalpituzumab Tesirine and Nivolumab + Ipilimumab

Reporting group description:

Participants received 2 doses of 0.3 mg/kg rovalpituzumab tesirine IV 6 weeks apart (Day 1 of Cycles 1 and 3), nivolumab 1 mg/kg every 3 weeks for 4 cycles beginning on Cycle 2 (Day 1 of Cycles 2-5), and ipilimumab 1 mg/kg IV every 3 weeks for 4 cycles beginning on Cycle 2 (Day 1 of Cycles 2-5).
After a 6-week washout, participants then received maintenance therapy with 480 mg nivolumab IV once every 4 weeks from Cycle 6 until disease progression.

Reporting group title	Cohort 1: Rovalpituzumab Tesirine and Nivolumab

Reporting group description:

Participants received 2 doses of 0.3 mg/kg rovalpituzumab tesirine by intravenous (IV) infusion 6 weeks apart (Day 1 of Cycles 1 and 3), and 2 doses of 360 mg nivolumab IV 3 weeks apart beginning on Cycle 2 (Day 1 of Cycles 2 and 3).
Participants then received maintenance therapy with 480 mg nivolumab IV once every 4 weeks from Cycle 4 until disease progression.

Serious adverse events	Cohort 2: Rovalpituzumab Tesirine and Nivolumab + Ipilimumab	Cohort 1: Rovalpituzumab Tesirine and Nivolumab	
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 12 (75.00%)	23 / 30 (76.67%)	
number of deaths (all causes)	8	26	
number of deaths resulting from adverse events	4	14	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
MALIGNANT NEOPLASM PROGRESSION			
subjects affected / exposed	2 / 12 (16.67%)	8 / 30 (26.67%)	
occurrences causally related to treatment / all	0 / 2	1 / 8	
deaths causally related to treatment / all	0 / 2	1 / 8	
Vascular disorders			
HYPOTENSION			

subjects affected / exposed	1 / 12 (8.33%)	0 / 30 (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			
CONDITION AGGRAVATED			
subjects affected / exposed	0 / 12 (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	
FACE OEDEMA			
subjects affected / exposed	0 / 12 (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	
FATIGUE			
subjects affected / exposed	2 / 12 (16.67%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
GENERALISED OEDEMA			
subjects affected / exposed	0 / 12 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
ACUTE RESPIRATORY DISTRESS SYNDROME			
subjects affected / exposed	0 / 12 (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	
ACUTE RESPIRATORY FAILURE			
subjects affected / exposed	0 / 12 (0.00%)	2 / 30 (6.67%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
DYSPNOEA			

subjects affected / exposed	0 / 12 (0.00%)	3 / 30 (10.00%)	
occurrences causally related to treatment / all	0 / 0	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPOXIA			
subjects affected / exposed	0 / 12 (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	
PLEURAL EFFUSION			
subjects affected / exposed	0 / 12 (0.00%)	8 / 30 (26.67%)	
occurrences causally related to treatment / all	0 / 0	11 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONITIS			
subjects affected / exposed	1 / 12 (8.33%)	3 / 30 (10.00%)	
occurrences causally related to treatment / all	1 / 1	6 / 6	
deaths causally related to treatment / all	0 / 0	2 / 2	
PNEUMOTHORAX			
subjects affected / exposed	0 / 12 (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 FAILURE			
subjects affected / exposed	0 / 12 (0.00%)	2 / 30 (6.67%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
BLOOD CREATININE INCREASED			
subjects affected / exposed	0 / 12 (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	
Injury, poisoning and procedural complications			
FEMORAL NECK FRACTURE			
subjects affected / exposed	0 / 12 (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	1 / 12 (8.33%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ATRIAL FIBRILLATION			
subjects affected / exposed	0 / 12 (0.00%)	2 / 30 (6.67%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
CARDIAC ARREST			
subjects affected / exposed	0 / 12 (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	
CARDIAC TAMPONADE			
subjects affected / exposed	0 / 12 (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	
MYOCARDIAL INFARCTION			
subjects affected / exposed	1 / 12 (8.33%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PERICARDIAL EFFUSION			
subjects affected / exposed	1 / 12 (8.33%)	2 / 30 (6.67%)	
occurrences causally related to treatment / all	1 / 1	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
TACHYCARDIA			
subjects affected / exposed	1 / 12 (8.33%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
ISCHAEMIC STROKE			
subjects affected / exposed	1 / 12 (8.33%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

PERONEAL NERVE PALSY			
subjects affected / exposed	1 / 12 (8.33%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
DISSEMINATED INTRAVASCULAR COAGULATION			
subjects affected / exposed	0 / 12 (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			
ASCITES			
subjects affected / exposed	0 / 12 (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	
COLITIS			
subjects affected / exposed	1 / 12 (8.33%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
AUTOIMMUNE HEPATITIS			
subjects affected / exposed	0 / 12 (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	
DRUG-INDUCED LIVER INJURY			
subjects affected / exposed	1 / 12 (8.33%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
HEPATOCELLULAR INJURY			
subjects affected / exposed	0 / 12 (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	
Skin and subcutaneous tissue disorders			
RASH MACULO-PAPULAR			

subjects affected / exposed	1 / 12 (8.33%)	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	0 / 12 (0.00%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Musculoskeletal and connective tissue disorders			
MUSCULAR WEAKNESS			
subjects affected / exposed	0 / 12 (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	
Infections and infestations			
EMPYEMA			
subjects affected / exposed	0 / 12 (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	
INFLUENZA			
subjects affected / exposed	1 / 12 (8.33%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
PNEUMONIA			
subjects affected / exposed	0 / 12 (0.00%)	2 / 30 (6.67%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
PNEUMONIA FUNGAL			
subjects affected / exposed	0 / 12 (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	
RESPIRATORY TRACT INFECTION BACTERIAL			

subjects affected / exposed	1 / 12 (8.33%)	0 / 30 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
SEPSIS			
subjects affected / exposed	1 / 12 (8.33%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SEPTIC SHOCK			
subjects affected / exposed	0 / 12 (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	
Metabolism and nutrition disorders			
DEHYDRATION			
subjects affected / exposed	2 / 12 (16.67%)	1 / 30 (3.33%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
HYPONATRAEMIA			
subjects affected / exposed	0 / 12 (0.00%)	2 / 30 (6.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Cohort 2: Rovalpituzumab Tesirine and Nivolumab + Ipilimumab	Cohort 1: Rovalpituzumab Tesirine and Nivolumab	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 12 (100.00%)	30 / 30 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
TUMOUR PAIN			
subjects affected / exposed	2 / 12 (16.67%)	0 / 30 (0.00%)	
occurrences (all)	2	0	
Vascular disorders			

FLUSHING			
subjects affected / exposed	1 / 12 (8.33%)	1 / 30 (3.33%)	
occurrences (all)	1	1	
HYPERTENSION			
subjects affected / exposed	0 / 12 (0.00%)	4 / 30 (13.33%)	
occurrences (all)	0	5	
HYPOTENSION			
subjects affected / exposed	1 / 12 (8.33%)	4 / 30 (13.33%)	
occurrences (all)	2	5	
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	3 / 12 (25.00%)	5 / 30 (16.67%)	
occurrences (all)	5	14	
CHEST PAIN			
subjects affected / exposed	2 / 12 (16.67%)	1 / 30 (3.33%)	
occurrences (all)	2	1	
FACE OEDEMA			
subjects affected / exposed	2 / 12 (16.67%)	6 / 30 (20.00%)	
occurrences (all)	2	8	
FATIGUE			
subjects affected / exposed	4 / 12 (33.33%)	11 / 30 (36.67%)	
occurrences (all)	5	14	
LOCALISED OEDEMA			
subjects affected / exposed	1 / 12 (8.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
MUCOSAL INFLAMMATION			
subjects affected / exposed	1 / 12 (8.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	0 / 12 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	2	
OEDEMA PERIPHERAL			
subjects affected / exposed	3 / 12 (25.00%)	12 / 30 (40.00%)	
occurrences (all)	4	18	
PAIN			

subjects affected / exposed	0 / 12 (0.00%)	3 / 30 (10.00%)	
occurrences (all)	0	4	
PYREXIA			
subjects affected / exposed	3 / 12 (25.00%)	5 / 30 (16.67%)	
occurrences (all)	3	7	
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	0 / 12 (0.00%)	3 / 30 (10.00%)	
occurrences (all)	0	4	
DYSPNOEA			
subjects affected / exposed	5 / 12 (41.67%)	11 / 30 (36.67%)	
occurrences (all)	5	17	
DYSPNOEA EXERTIONAL			
subjects affected / exposed	1 / 12 (8.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
HICCUPS			
subjects affected / exposed	1 / 12 (8.33%)	1 / 30 (3.33%)	
occurrences (all)	1	2	
HYPOXIA			
subjects affected / exposed	1 / 12 (8.33%)	0 / 30 (0.00%)	
occurrences (all)	2	0	
OROPHARYNGEAL PAIN			
subjects affected / exposed	1 / 12 (8.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
PLEURAL EFFUSION			
subjects affected / exposed	5 / 12 (41.67%)	7 / 30 (23.33%)	
occurrences (all)	7	13	
PRODUCTIVE COUGH			
subjects affected / exposed	2 / 12 (16.67%)	2 / 30 (6.67%)	
occurrences (all)	2	2	
PULMONARY HYPERTENSION			
subjects affected / exposed	1 / 12 (8.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
RHINORRHOEA			

subjects affected / exposed	1 / 12 (8.33%)	1 / 30 (3.33%)	
occurrences (all)	2	1	
WHEEZING			
subjects affected / exposed	0 / 12 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	2	
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	0 / 12 (0.00%)	3 / 30 (10.00%)	
occurrences (all)	0	3	
CONFUSIONAL STATE			
subjects affected / exposed	1 / 12 (8.33%)	2 / 30 (6.67%)	
occurrences (all)	1	2	
DEPRESSION			
subjects affected / exposed	1 / 12 (8.33%)	0 / 30 (0.00%)	
occurrences (all)	2	0	
INSOMNIA			
subjects affected / exposed	0 / 12 (0.00%)	4 / 30 (13.33%)	
occurrences (all)	0	6	
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 12 (0.00%)	3 / 30 (10.00%)	
occurrences (all)	0	6	
AMYLASE INCREASED			
subjects affected / exposed	0 / 12 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	3	
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	0 / 12 (0.00%)	4 / 30 (13.33%)	
occurrences (all)	0	5	
BLOOD ALKALINE PHOSPHATASE INCREASED			
subjects affected / exposed	0 / 12 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	5	
BLOOD BILIRUBIN INCREASED			
subjects affected / exposed	0 / 12 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	4	
BLOOD CREATINE PHOSPHOKINASE			

INCREASED			
subjects affected / exposed	1 / 12 (8.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
BLOOD CREATININE INCREASED			
subjects affected / exposed	1 / 12 (8.33%)	2 / 30 (6.67%)	
occurrences (all)	1	2	
BLOOD LACTATE DEHYDROGENASE INCREASED			
subjects affected / exposed	0 / 12 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	2	
BLOOD THYROID STIMULATING HORMONE DECREASED			
subjects affected / exposed	0 / 12 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	2	
Injury, poisoning and procedural complications			
CONTUSION			
subjects affected / exposed	1 / 12 (8.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
FALL			
subjects affected / exposed	1 / 12 (8.33%)	1 / 30 (3.33%)	
occurrences (all)	1	1	
Cardiac disorders			
ATRIAL FIBRILLATION			
subjects affected / exposed	0 / 12 (0.00%)	3 / 30 (10.00%)	
occurrences (all)	0	3	
PALPITATIONS			
subjects affected / exposed	1 / 12 (8.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
PERICARDIAL EFFUSION			
subjects affected / exposed	1 / 12 (8.33%)	7 / 30 (23.33%)	
occurrences (all)	2	8	
SINUS TACHYCARDIA			
subjects affected / exposed	0 / 12 (0.00%)	3 / 30 (10.00%)	
occurrences (all)	0	3	
TACHYCARDIA			
subjects affected / exposed	1 / 12 (8.33%)	2 / 30 (6.67%)	
occurrences (all)	2	2	

Nervous system disorders			
DIZZINESS			
subjects affected / exposed	1 / 12 (8.33%)	2 / 30 (6.67%)	
occurrences (all)	1	2	
DYSGEUSIA			
subjects affected / exposed	0 / 12 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	3	
HEADACHE			
subjects affected / exposed	0 / 12 (0.00%)	6 / 30 (20.00%)	
occurrences (all)	0	6	
HEMIPARESIS			
subjects affected / exposed	1 / 12 (8.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
HYPERAESTHESIA			
subjects affected / exposed	1 / 12 (8.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
NEURALGIA			
subjects affected / exposed	1 / 12 (8.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	6 / 12 (50.00%)	10 / 30 (33.33%)	
occurrences (all)	6	17	
LEUKOCYTOSIS			
subjects affected / exposed	1 / 12 (8.33%)	1 / 30 (3.33%)	
occurrences (all)	1	1	
LYMPHOPENIA			
subjects affected / exposed	0 / 12 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	2	
NEUTROPENIA			
subjects affected / exposed	2 / 12 (16.67%)	1 / 30 (3.33%)	
occurrences (all)	2	1	
THROMBOCYTOPENIA			
subjects affected / exposed	5 / 12 (41.67%)	9 / 30 (30.00%)	
occurrences (all)	7	14	
Eye disorders			

CATARACT			
subjects affected / exposed	1 / 12 (8.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
DRY EYE			
subjects affected / exposed	1 / 12 (8.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
EYE PRURITUS			
subjects affected / exposed	1 / 12 (8.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
EYELID OEDEMA			
subjects affected / exposed	1 / 12 (8.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
OCULAR HYPERAEMIA			
subjects affected / exposed	1 / 12 (8.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
PERIORBITAL OEDEMA			
subjects affected / exposed	1 / 12 (8.33%)	2 / 30 (6.67%)	
occurrences (all)	1	2	
RETINOPATHY			
subjects affected / exposed	1 / 12 (8.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
VISION BLURRED			
subjects affected / exposed	1 / 12 (8.33%)	1 / 30 (3.33%)	
occurrences (all)	1	1	
VISUAL IMPAIRMENT			
subjects affected / exposed	1 / 12 (8.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
XEROPHTHALMIA			
subjects affected / exposed	1 / 12 (8.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
ABDOMINAL DISTENSION			
subjects affected / exposed	0 / 12 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	2	
ABDOMINAL PAIN			

subjects affected / exposed	2 / 12 (16.67%)	7 / 30 (23.33%)	
occurrences (all)	2	7	
ABDOMINAL PAIN UPPER			
subjects affected / exposed	0 / 12 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	2	
ASCITES			
subjects affected / exposed	2 / 12 (16.67%)	1 / 30 (3.33%)	
occurrences (all)	4	1	
COLITIS			
subjects affected / exposed	1 / 12 (8.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
CONSTIPATION			
subjects affected / exposed	3 / 12 (25.00%)	8 / 30 (26.67%)	
occurrences (all)	3	9	
DIARRHOEA			
subjects affected / exposed	4 / 12 (33.33%)	4 / 30 (13.33%)	
occurrences (all)	4	4	
DRY MOUTH			
subjects affected / exposed	2 / 12 (16.67%)	0 / 30 (0.00%)	
occurrences (all)	2	0	
ERUCTATION			
subjects affected / exposed	1 / 12 (8.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
GASTROOESOPHAGEAL REFLUX DISEASE			
subjects affected / exposed	1 / 12 (8.33%)	2 / 30 (6.67%)	
occurrences (all)	1	2	
LIP DRY			
subjects affected / exposed	1 / 12 (8.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
NAUSEA			
subjects affected / exposed	1 / 12 (8.33%)	5 / 30 (16.67%)	
occurrences (all)	1	6	
RETCHING			
subjects affected / exposed	1 / 12 (8.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	

VOMITING			
subjects affected / exposed	3 / 12 (25.00%)	7 / 30 (23.33%)	
occurrences (all)	3	10	
Hepatobiliary disorders			
HEPATIC FUNCTION ABNORMAL			
subjects affected / exposed	1 / 12 (8.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
HEPATOCELLULAR INJURY			
subjects affected / exposed	1 / 12 (8.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
LIVER INJURY			
subjects affected / exposed	0 / 12 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	2	
Skin and subcutaneous tissue disorders			
BLISTER			
subjects affected / exposed	2 / 12 (16.67%)	1 / 30 (3.33%)	
occurrences (all)	2	1	
DRY SKIN			
subjects affected / exposed	0 / 12 (0.00%)	3 / 30 (10.00%)	
occurrences (all)	0	3	
ERYTHEMA			
subjects affected / exposed	2 / 12 (16.67%)	6 / 30 (20.00%)	
occurrences (all)	2	8	
PHOTOSENSITIVITY REACTION			
subjects affected / exposed	2 / 12 (16.67%)	7 / 30 (23.33%)	
occurrences (all)	4	10	
PRURITUS			
subjects affected / exposed	3 / 12 (25.00%)	1 / 30 (3.33%)	
occurrences (all)	4	1	
PRURITUS GENERALISED			
subjects affected / exposed	1 / 12 (8.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
RASH			
subjects affected / exposed	1 / 12 (8.33%)	1 / 30 (3.33%)	
occurrences (all)	2	1	
RASH MACULAR			

subjects affected / exposed	1 / 12 (8.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
RASH MACULO-PAPULAR			
subjects affected / exposed	4 / 12 (33.33%)	5 / 30 (16.67%)	
occurrences (all)	6	5	
SUBACUTE CUTANEOUS LUPUS ERYTHEMATOSUS			
subjects affected / exposed	1 / 12 (8.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
PROTEINURIA			
subjects affected / exposed	0 / 12 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	2	
Endocrine disorders			
HYPERTHYROIDISM			
subjects affected / exposed	1 / 12 (8.33%)	1 / 30 (3.33%)	
occurrences (all)	1	2	
HYPOTHYROIDISM			
subjects affected / exposed	2 / 12 (16.67%)	3 / 30 (10.00%)	
occurrences (all)	2	3	
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	1 / 12 (8.33%)	5 / 30 (16.67%)	
occurrences (all)	2	7	
BACK PAIN			
subjects affected / exposed	0 / 12 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	2	
FLANK PAIN			
subjects affected / exposed	0 / 12 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	3	
MUSCULOSKELETAL PAIN			
subjects affected / exposed	0 / 12 (0.00%)	4 / 30 (13.33%)	
occurrences (all)	0	4	
MYALGIA			
subjects affected / exposed	2 / 12 (16.67%)	1 / 30 (3.33%)	
occurrences (all)	2	1	
NECK PAIN			

subjects affected / exposed	0 / 12 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	2	
PAIN IN EXTREMITY			
subjects affected / exposed	1 / 12 (8.33%)	2 / 30 (6.67%)	
occurrences (all)	1	2	
Infections and infestations			
BRONCHITIS			
subjects affected / exposed	0 / 12 (0.00%)	3 / 30 (10.00%)	
occurrences (all)	0	3	
CONJUNCTIVITIS			
subjects affected / exposed	2 / 12 (16.67%)	1 / 30 (3.33%)	
occurrences (all)	2	1	
HORDEOLUM			
subjects affected / exposed	1 / 12 (8.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
ORAL CANDIDIASIS			
subjects affected / exposed	1 / 12 (8.33%)	3 / 30 (10.00%)	
occurrences (all)	1	3	
PNEUMONIA BACTERIAL			
subjects affected / exposed	1 / 12 (8.33%)	1 / 30 (3.33%)	
occurrences (all)	2	1	
SINUSITIS			
subjects affected / exposed	1 / 12 (8.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
SKIN BACTERIAL INFECTION			
subjects affected / exposed	1 / 12 (8.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
URINARY TRACT INFECTION			
subjects affected / exposed	2 / 12 (16.67%)	4 / 30 (13.33%)	
occurrences (all)	2	5	
VIRAL INFECTION			
subjects affected / exposed	1 / 12 (8.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
DECREASED APPETITE			

subjects affected / exposed	5 / 12 (41.67%)	9 / 30 (30.00%)	
occurrences (all)	6	11	
DEHYDRATION			
subjects affected / exposed	2 / 12 (16.67%)	0 / 30 (0.00%)	
occurrences (all)	2	0	
HYPERCALCAEMIA			
subjects affected / exposed	1 / 12 (8.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
HYPERGLYCAEMIA			
subjects affected / exposed	1 / 12 (8.33%)	4 / 30 (13.33%)	
occurrences (all)	1	4	
HYPERKALAEMIA			
subjects affected / exposed	1 / 12 (8.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
HYPERLIPASAEMIA			
subjects affected / exposed	0 / 12 (0.00%)	2 / 30 (6.67%)	
occurrences (all)	0	3	
HYPERPHOSPHATAEMIA			
subjects affected / exposed	1 / 12 (8.33%)	0 / 30 (0.00%)	
occurrences (all)	1	0	
HYPOALBUMINAEMIA			
subjects affected / exposed	2 / 12 (16.67%)	6 / 30 (20.00%)	
occurrences (all)	2	10	
HYPOCALCAEMIA			
subjects affected / exposed	1 / 12 (8.33%)	1 / 30 (3.33%)	
occurrences (all)	1	1	
HYPOKALAEMIA			
subjects affected / exposed	0 / 12 (0.00%)	5 / 30 (16.67%)	
occurrences (all)	0	5	
HYPOMAGNESAEMIA			
subjects affected / exposed	1 / 12 (8.33%)	4 / 30 (13.33%)	
occurrences (all)	1	4	
HYPONATRAEMIA			
subjects affected / exposed	2 / 12 (16.67%)	3 / 30 (10.00%)	
occurrences (all)	6	3	
HYPOPHOSPHATAEMIA			

subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	3 / 30 (10.00%) 3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 December 2016	Defined target level of activity based on overall response rate (ORR) that would help inform decisions on program development; clarification of contraception recommendations; recommendations provided in the Study May Proceed Memorandum dated 08 December 2016 were added, including updated Day 2 assessments for PK and additional PK and anti-therapeutic antibody-related analytes of rovalpituzumab tesirine; and other administrative corrections and clarifications.
01 December 2017	Most amendment changes were revisions to enhance recruitment; these included clarifications to the prior therapy eligibility requirements and simultaneous cohort enrollment. Additionally, the following items were clarified: dosing schedules; required premedication and post-medication; blood tumor markers and biomarkers collection; the DLT evaluation period; dose delay criteria; washout period and telephone follow-up procedures; radiographic assessment; and permanent treatment discontinuation criteria including treatment continuation beyond progression and dosing interruption; and other administrative corrections and clarifications.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported