



Clinical trial results:

An Open-label, Single-Arm, Phase 2 Study Evaluating the Efficacy, Safety and Pharmacokinetics of Rovalpituzumab Tesirine (SC16LD6.5) for Third-line and Later Treatment of Subjects With Relapsed or Refractory Delta-Like Protein 3-Expressing Small Cell Lung Cancer (TRINITY)

Summary

EudraCT number	2015-004506-42
Trial protocol	HU DE ES PL
Global end of trial date	19 October 2018

Results information

Result version number	v1
This version publication date	16 October 2019
First version publication date	16 October 2019

Trial information

Trial identification

Sponsor protocol code	SCRX001-002
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02674568
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AbbVie Deutschland GmbH & Co.KG
Sponsor organisation address	AbbVie House, Vanwall Business Park, Vanwall Road, Maidenhead, Berkshire, United States, SL6-4UB
Public contact	Philip Komarnitsky, Group Medical Director, Abbvie, 1 617 252 4747, philip.komarnitsky@abbvie.com
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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	19 October 2018
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	19 October 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to investigate the efficacy of rovalpituzumab tesirine as third-line and later (3L+) treatment for subjects with relapsed or refractory DLL3-expressing small cell lung cancer (SCLC) as measured by objective response rate and overall survival.

Protection of trial subjects:

Participant and/or legal guardian read and understood the information provided about the study and gave written permission.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 January 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 202
Country: Number of subjects enrolled	France: 56
Country: Number of subjects enrolled	Germany: 37
Country: Number of subjects enrolled	Hungary: 8
Country: Number of subjects enrolled	Poland: 6
Country: Number of subjects enrolled	Spain: 33
Worldwide total number of subjects	342
EEA total number of subjects	140

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)	204
From 65 to 84 years	135
85 years and over	3

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Screening assessments were completed within 14 days of the Day 1 visit.

Pre-assignment period milestones

Number of subjects started	342
Number of subjects completed	339

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Enrolled but not dosed: 3
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Period 1

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

Arms

Arm title	Rovalpituzumab Tesirine
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Arm description:

0.3 mg/kg rovalpituzumab tesirine administered intravenously on Day 1 of each 42-day cycle (every 6 weeks; Q6W) for 2 cycles. An additional 2 cycles of rovalpituzumab tesirine (retreatment) was permitted for eligible subjects.

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:

Dosing is based on subject actual body weight to the nearest tenth of a kilogram, assessed on Day 1 of each cycle, and administered according to the assigned dose.

Number of subjects in period 1 ^[1]	Rovalpituzumab Tesirine
Started	339
Delta-like Protein 3 (DLL3) High	238
DLL3 Positive	287
Completed	0
Not completed	339
Consent withdrawn by subject	5
Physician decision	2

Death	303
Lost to follow-up	9
Other, Not Specified	20

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: A total of 342 subjects were enrolled; 3 subjects were not dosed.

Baseline characteristics

Reporting groups

Reporting group title	Rovalpituzumab Tesirine
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Reporting group description:

0.3 mg/kg rovalpituzumab tesirine administered intravenously on Day 1 of each 42-day cycle (every 6 weeks; Q6W) for 2 cycles. An additional 2 cycles of rovalpituzumab tesirine (retreatment) was permitted for eligible subjects.

Reporting group values	Rovalpituzumab Tesirine	Total	
Number of subjects	339	339	
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	61.9 ± 9.36	-	
Gender categorical Units: Subjects			
Female	169	169	
Male	170	170	
Race Units: Subjects			
American Indian or Alaska Native	1	1	
Asian	3	3	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	11	11	
White	265	265	
More than one race	3	3	
Unknown or Not Reported	56	56	
Ethnicity Units: Subjects			
Hispanic or Latino	10	10	
Not Hispanic or Latino	272	272	
Unknown or Not Reported	57	57	

End points

End points reporting groups

Reporting group title	Rovalpituzumab Tesirine
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Reporting group description:

0.3 mg/kg rovalpituzumab tesirine administered intravenously on Day 1 of each 42-day cycle (every 6 weeks; Q6W) for 2 cycles. An additional 2 cycles of rovalpituzumab tesirine (retreatment) was permitted for eligible subjects.

Subject analysis set title	Rovalpituzumab Tesirine: DLL3 High
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Subject analysis set type	Modified intention-to-treat
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Subject analysis set description:

Modified Intent to Treat Population: all subjects who received any amount of study drug.

'DLL3 High' (tumors with $\geq 75\%$ of cells expressing DLL3) participants received 0.3 mg/kg rovalpituzumab tesirine administered intravenously on Day 1 of each 42-day cycle (Q6W) for 2 cycles. An additional 2 cycles of rovalpituzumab tesirine (retreatment) was permitted for eligible subjects.

Subject analysis set title	Rovalpituzumab Tesirine: DLL3 Positive
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Subject analysis set type	Modified intention-to-treat
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Subject analysis set description:

Modified Intent to Treat Population: all subjects who received any amount of study drug.

'DLL3 Positive' (tumors with $\geq 25\%$ of cells expressing DLL3) subjects received 0.3 mg/kg rovalpituzumab tesirine administered intravenously on Day 1 of each 42-day cycle (Q6W) for 2 cycles. An additional 2 cycles of rovalpituzumab tesirine (retreatment) was permitted for eligible subjects.

Subject analysis set title	Pharmacokinetic Analysis Population: Initial Treatment Period
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Subject analysis set type	Full analysis
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Subject analysis set description:

Pharmacokinetic Analysis Population: all subjects who receive at least 1 dose of study treatment and at least 1 post-baseline blood sample following a dose of study treatment.

Initial Treatment Period: 0.3 mg/kg rovalpituzumab tesirine administered intravenously on Day 1 of each 42-day cycle (Q6W) for 2 cycles.

Subject analysis set title	Pharmacokinetic Analysis Population: Re-Treatment 1
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Subject analysis set type	Full analysis
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Subject analysis set description:

Pharmacokinetic Analysis Population: all subjects who receive at least 1 dose of study treatment and at least 1 post-baseline blood sample following a dose of study treatment.

Re-Treatment 1: 0.3 mg/kg rovalpituzumab tesirine administered intravenously on Day 1 of retreatment Cycle 1.

Subject analysis set title	Pharmacokinetic Analysis Population: Re-Treatment 2
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Subject analysis set type	Full analysis
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Subject analysis set description:

Pharmacokinetic Analysis Population: all subjects who receive at least 1 dose of study treatment and at least 1 post-baseline blood sample following a dose of study treatment.

Re-Treatment 2: 0.3 mg/kg rovalpituzumab tesirine administered intravenously on Day 1 of retreatment Cycle 2.

Primary: Objective Response Rate

End point title	Objective Response Rate ^[1]
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End point description:

Objective response is defined as a subject with the best overall response of complete response (CR) or partial response (PR), per Response Evaluation Criteria in Solid Tumors (RECIST) v 1.1, prior to receiving any subsequent anticancer therapy and retreatment, and is confirmed by a consecutive response assessment at least 4 weeks (28 days) from the initial determination of CR/PR. Analyzed

based on response assessments from both the Independent Review Committee (IRC) and investigators.
CR: disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to <10 mm.

PR: at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters.

End point type	Primary
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End point timeframe:

up to 122.4 weeks; mean (SD) duration of follow-up was 29.0 (23.77) 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: Statistics are presented per protocol.

End point values	Rovalpituzumab b Tesirine: DLL3 High	Rovalpituzumab b Tesirine: DLL3 Positive		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	238	287		
Units: percentage of subjects				
number (confidence interval 95%)				
IRC	15.5 (11.2 to 20.8)	14.6 (10.8 to 19.3)		
Investigator	19.3 (14.5 to 24.9)	18.8 (14.5 to 23.8)		

Statistical analyses

No statistical analyses for this end point

Primary: Overall Survival

End point title	Overall Survival ^[2]
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End point description:

Overall survival is defined as the time from the first dose date to death for any reason. Subjects who were alive at the clinical data cut-off were censored at the last known alive date. Based on Kaplan-Meier estimates.

End point type	Primary
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End point timeframe:

up to 122.4 weeks; mean (SD) duration of follow-up was 29.0 (23.77) weeks

Notes:

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

Justification: Statistics are presented per protocol.

End point values	Rovalpituzumab b Tesirine: DLL3 High	Rovalpituzumab b Tesirine: DLL3 Positive		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	238	287		
Units: months				
median (confidence interval 95%)	5.3 (4.7 to 5.8)	5.3 (4.7 to 5.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Response Rate

End point title	Overall Response Rate
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End point description:

Overall response rate is defined as the percentage of subjects with a response of CR or PR, regardless of confirmation, per RECIST v 1.1 prior to receiving any subsequent anticancer therapy and retreatment. Any participants not exhibiting a response (CR or PR) as defined above were considered non-responders. Analyzed based on response assessments from both the IRC and investigators.

CR: disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to <10 mm.

PR: at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters.

End point type	Secondary
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End point timeframe:

up to 122.4 weeks; mean (SD) duration of follow-up was 29.0 (23.77) weeks

End point values	Rovalpituzuma b Tesirine: DLL3 High	Rovalpituzuma b Tesirine: DLL3 Positive		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	238	287		
Units: percentage of subjects				
number (confidence interval 95%)				
IRC	23.1 (17.9 to 29.0)	22.0 (17.3 to 27.2)		
Investigator	26.9 (21.4 to 33.0)	25.8 (20.8 to 31.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Objective Response

End point title	Duration of Objective Response
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End point description:

Duration of objective response is defined as the time from the date of first documented CR or PR of subjects with a confirmed response to the documented date of progressive disease (PD) or death, whichever occurred first. Subjects who neither progressed nor died are censored at the last evaluable disease assessment. Analyzed based on response assessments from both the IRC and investigators. Based on Kaplan-Meier estimates.

CR: disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to <10 mm.

PR: at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters.

PD: at least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study (includes the baseline sum). The sum must also demonstrate an absolute increase of at least 5 mm. (The appearance of one or more new lesions is also considered progression.)

End point type	Secondary
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End point timeframe:

up to 122.4 weeks; mean (SD) duration of follow-up was 29.0 (23.77) weeks

End point values	Rovalpituzuma b Tesirine: DLL3 High	Rovalpituzuma b Tesirine: DLL3 Positive		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	46 ^[3]	54		
Units: months				
median (confidence interval 95%)				
IRC; n=37, 42	4.0 (3.0 to 4.2)	4.1 (3.0 to 4.2)		
Investigator; n=46, 54	4.0 (2.9 to 4.2)	4.0 (2.9 to 4.3)		

Notes:

[3] - n=subjects who had an objective response

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival

End point title	Progression-Free Survival
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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. Subjects who neither progressed nor died were censored at the last evaluable disease assessment. Analyzed based on response assessments from both the IRC and investigators. Based on Kaplan-Meier estimates.

PD: at least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study (includes the baseline sum). The sum must also demonstrate an absolute increase of at least 5 mm. (The appearance of one or more new lesions is also considered progression.)

End point type	Secondary
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End point timeframe:

up to 122.4 weeks; mean (SD) duration of follow-up was 29.0 (23.77) weeks

End point values	Rovalpituzuma b Tesirine: DLL3 High	Rovalpituzuma b Tesirine: DLL3 Positive		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	238	287		
Units: months				
median (confidence interval 95%)				
IRC	3.8 (3.3 to 4.1)	3.8 (3.3 to 4.0)		
Investigator	3.9 (3.3 to 4.1)	3.9 (3.3 to 4.0)		

Statistical analyses

Secondary: Clinical Benefit Rate

End point title	Clinical Benefit Rate
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End point description:

Clinical benefit rate is defined as the proportion of subjects with an overall response of CR or PR or stable disease (SD) with SD of a minimum duration of 42 days from the first dose date. Analyzed based on response assessments from both the IRC and investigators.

CR: disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to <10 mm.

PR: at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters.

SD: neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference the smallest sum diameters while on study.

PD: at least a 20% increase in the sum of diameters of target lesions, taking as reference the smallest sum on study (includes the baseline sum). The sum must also demonstrate an absolute increase of at least 5 mm. (The appearance of one or more new lesions is also considered progression.)

End point type	Secondary
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End point timeframe:

up to 122.4 weeks; mean (SD) duration of follow-up was 29.0 (23.77) weeks

End point values	Rovalpituzumab b Tesirine: DLL3 High	Rovalpituzumab b Tesirine: DLL3 Positive		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	238	287		
Units: percentage of subjects				
number (confidence interval 95%)				
IRC	73.9 (67.9 to 79.4)	72.1 (66.6 to 77.2)		
Investigator	71.0 (64.8 to 76.7)	68.6 (62.9 to 74.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Clinical Benefit

End point title	Duration of Clinical Benefit
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End point description:

Duration of clinical benefit is defined as the time from the date of first documented CR or PR or SD of \geq 42 days from first dose date (-7 days to allow for scheduled visit window per the protocol) to the documented date PD or death, whichever occurs first. Analyzed based on response assessments from both the IRC and investigators.

CR: disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to <10 mm.

PR: at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters.

SD: neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference the smallest sum diameters while on study.

End point type	Secondary
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End point timeframe:

up to 122.4 weeks; mean (SD) duration of follow-up was 29.0 (23.77) weeks

End point values	Rovalpituzumab b Tesirine: DLL3 High	Rovalpituzumab b Tesirine: DLL3 Positive		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	176 ^[4]	207 ^[5]		
Units: months				
median (confidence interval 95%)				
IRC; n=176, 207	2.9 (2.8 to 3.2)	2.9 (2.8 to 3.0)		
Investigator; n=169, 197	3.0 (2.9 to 3.3)	3.0 (2.9 to 3.2)		

Notes:

[4] - n= subjects with best overall response of CR or PR or SD

[5] - n= subjects with best overall response of CR or PR or SD

Statistical analyses

No statistical analyses for this end point

Secondary: Rovalpituzumab Tesirine Antibody-Drug Conjugate Plasma Concentrations by Study Visit

End point title	Rovalpituzumab Tesirine Antibody-Drug Conjugate Plasma Concentrations by Study Visit
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End point description:

End point type	Secondary
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End point timeframe:

Cycle 1: Day 1, 30 minutes pre-infusion; Day 1, 30 minutes post-infusion; Day 3; Day 15; Day 29.

Cycle 2: Day 1, 30 minutes pre-infusion; Day 1, 30 minutes post-infusion; Day 3; Day 15; Day 29; End of Treatment (up to Day 29).

End point values	Pharmacokinetic Analysis Population: Initial Treatment Period	Pharmacokinetic Analysis Population: Re- Treatment 1	Pharmacokinetic Analysis Population: Re- Treatment 2	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	329 ^[6]	20 ^[7]	2 ^[8]	
Units: ng/mL				
arithmetic mean (standard deviation)				
Cycle 1: Day 1, 30 mins pre-infusion; n=329,20,2	180.9 (± 1215.03)	136.6 (± 923.44)	148.2 (± 81.81)	
Cycle 1: Day 1, 30 mins post-infusion; n=329,20,2	7611.6 (± 1980.49)	6365.5 (± 1763.08)	6690.0 (± 2050.61)	
Cycle 1: Day 3; n=317,20,2	4535.2 (± 1398.49)	3740.5 (± 1454.87)	4630.0 (± 1866.76)	
Cycle 1: Day 15; n=300,15,2	1472.8 (± 573.90)	1323.3 (± 504.33)	1390.0 (± 381.84)	

Cycle 1: Day 29; n=279,18,2	816.3 (± 379.15)	793.8 (± 322.90)	956.5 (± 61.52)	
Cycle 2: Day 1, 30 mins pre-infusion; n=223,15,1	532.2 (± 592.90)	518.6 (± 226.45)	601.0 (± 99999)	
Cycle 2: Day 1, 30 mins post-infusion; n=216,15,1	7535.6 (± 1928.74)	6602.7 (± 1508.23)	7880.0 (± 99999)	
Cycle 2: Day 3; n=205,13,1	4791.1 (± 1373.70)	4670.8 (± 1539.65)	3840.0 (± 99999)	
Cycle 2: Day 15; n=206,13,1	1845.5 (± 688.47)	1857.7 (± 599.65)	2030.0 (± 99999)	
Cycle 2: Day 29; n=175,14,1	1029.3 (± 362.28)	1077.7 (± 362.33)	1300.0 (± 99999)	
End of Treatment; n=213,15,2	558.5 (± 296.09)	686.9 (± 354.68)	679.5 (± 64.35)	

Notes:

[6] - n=subjects with an assessment at given time point

[7] - n=subjects with an assessment at given time point

[8] - n=subjects with an assessment at given time point. 99999=not applicable (1 subject analyzed)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Anti-Therapeutic Antibody (ATA) Positive Subjects

End point title	Number of Anti-Therapeutic Antibody (ATA) Positive Subjects
End point description:	
All subjects who received rovalpituzumab tesirine and had at least one sample screened for ATA against rovalpituzumab tesirine antibody-drug conjugate (ADC) concentration.	
End point type	Secondary
End point timeframe:	
up to 122.4 weeks; mean (SD) duration of follow-up was 29.0 (23.77) weeks	

End point values	Rovalpituzumab Tesirine			
Subject group type	Reporting group			
Number of subjects analysed	336 ^[9]			
Units: subjects				
Positive at any study visit; n=336	11			
Positive after first dose of study drug; n=276	3			

Notes:

[9] - n=subjects with ≥ 1 sample screened for ATA against rovalpituzumab tesirine ADC concentration

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment-Related Adverse Events (TEAEs) During Initial Treatment

End point title	Number of Subjects With Treatment-Related Adverse Events (TEAEs) During Initial Treatment
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End point description:

An adverse event (AE) is defined as any untoward medical occurrence which does not necessarily have a causal relationship with this treatment. A serious adverse event (SAE) is any untoward medical occurrence that at any dose: is fatal or life-threatening; results in death or hospitalization; is disabling/incapacitating or a congenital anomaly/birth defect; is medically significant. AE severity was graded using the National Cancer Institute's Common Terminology Criteria for Adverse Events (NCI CTCAE), version 4.03 terminology: grade 1=mild; grade 2=moderate; grade 3=severe; grade 4 life-threatening; grade 5=death. TEAEs were defined as AEs that were newly occurring or worsened following study treatment.

End point type	Secondary
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End point timeframe:

From first dose of study drug through the end of the initial treatment period (84 ± 6 days)

End point values	Rovalpituzumab Tesirine			
Subject group type	Reporting group			
Number of subjects analysed	339			
Units: subjects				
Any TEAE	335			
Treatment emergent SAE	171			
TEAE maximum severity grade 3/4	179			
TEAE leading to drug withdrawal	25			
TEAE leading to dose interruption	33			
TEAE leading to dose reduction	32			
TEAE reasonably possibly related to study drug	308			
Fatal AE	34			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With TEAEs Occurring in at Least 10% of All Participants During Initial Treatment

End point title	Number of Subjects With TEAEs Occurring in at Least 10% of All Participants During Initial Treatment
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End point description:

TEAEs were defined as AEs that were newly occurring or worsened following study treatment.

End point type	Secondary
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End point timeframe:

From first dose of study drug through the end of the initial treatment period (84 ± 6 days)

End point values	Rovalpituzumab Tesirine			
Subject group type	Reporting group			
Number of subjects analysed	339			
Units: subjects				
Any TEAE	335			
Fatigue	129			
Photosensitivity reaction	123			
Pleural effusion	113			
Oedema peripheral	105			
Decreased appetite	102			
Nausea	88			
Dyspnoea	83			
Thrombocytopenia	83			
Constipation	75			
Vomiting	59			
Anaemia	58			
Cough	54			
Hypoalbuminaemia	52			
Pericardial effusion	50			
Abdominal pain	50			
Asthenia	50			
Diarrhoea	47			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug through the end of treatment (EOT; 42 ± 3 days after last dose, or within 7 days of documentation of the decision to discontinue treatment, whichever was later) or 30 days after last study treatment, whichever was later.

Adverse event reporting additional description:

Mean (SD) duration of follow-up (ie, from the first dose date to the last known date alive or death date) was 29.0 (23.77) weeks.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	19
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Reporting groups

Reporting group title	Rovalpituzumab Tesirine
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Reporting group description:

0.3 mg/kg rovalpituzumab tesirine administered intravenously on Day 1 of each 42-day cycle (Q6W) for 2 cycles. An additional 2 cycles of rovalpituzumab tesirine (retreatment) was permitted for eligible subjects.

Serious adverse events	Rovalpituzumab Tesirine		
Total subjects affected by serious adverse events			
subjects affected / exposed	178 / 339 (52.51%)		
number of deaths (all causes)	303		
number of deaths resulting from adverse events	35		
Neoplasms benign, malignant and unspecified (incl cysts and polyps) MALIGNANT NEOPLASM PROGRESSION			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
METASTASES TO PANCREAS			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
METASTASIS			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Vascular disorders			
CAPILLARY LEAK SYNDROME			
subjects affected / exposed	2 / 339 (0.59%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
DEEP VEIN THROMBOSIS			
subjects affected / exposed	2 / 339 (0.59%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
HAEMORRHAGE			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
HYPERTENSION			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
HYPOTENSION			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
INTERMITTENT CLAUDICATION			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
ORTHOSTATIC HYPOTENSION			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
PERIPHERAL ISCHAEMIA			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
SUPERIOR VENA CAVA SYNDROME			

subjects affected / exposed	3 / 339 (0.88%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
VENOUS THROMBOSIS LIMB			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	4 / 339 (1.18%)		
occurrences causally related to treatment / all	4 / 6		
deaths causally related to treatment / all	0 / 1		
FATIGUE			
subjects affected / exposed	5 / 339 (1.47%)		
occurrences causally related to treatment / all	3 / 5		
deaths causally related to treatment / all	0 / 0		
GAIT DISTURBANCE			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
GENERAL PHYSICAL HEALTH DETERIORATION			
subjects affected / exposed	8 / 339 (2.36%)		
occurrences causally related to treatment / all	2 / 14		
deaths causally related to treatment / all	0 / 6		
GENERALISED OEDEMA			
subjects affected / exposed	8 / 339 (2.36%)		
occurrences causally related to treatment / all	10 / 10		
deaths causally related to treatment / all	2 / 2		
OEDEMA PERIPHERAL			
subjects affected / exposed	8 / 339 (2.36%)		
occurrences causally related to treatment / all	10 / 10		
deaths causally related to treatment / all	0 / 0		
PAIN			

subjects affected / exposed	3 / 339 (0.88%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
PYREXIA			
subjects affected / exposed	3 / 339 (0.88%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
ACUTE RESPIRATORY FAILURE			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
CHRONIC OBSTRUCTIVE PULMONARY DISEASE			
subjects affected / exposed	2 / 339 (0.59%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
DYSPNOEA			
subjects affected / exposed	4 / 339 (1.18%)		
occurrences causally related to treatment / all	2 / 4		
deaths causally related to treatment / all	0 / 1		
DYSPNOEA EXERTIONAL			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
HAEMOPTYSIS			
subjects affected / exposed	2 / 339 (0.59%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
HAEMOTHORAX			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
HYPOXIA			

subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
OBSTRUCTIVE AIRWAYS DISORDER			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
PLEURAL EFFUSION			
subjects affected / exposed	49 / 339 (14.45%)		
occurrences causally related to treatment / all	54 / 62		
deaths causally related to treatment / all	1 / 3		
PLEURISY			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
PNEUMONIA ASPIRATION			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
PNEUMONITIS			
subjects affected / exposed	2 / 339 (0.59%)		
occurrences causally related to treatment / all	5 / 5		
deaths causally related to treatment / all	1 / 1		
PNEUMOTHORAX			
subjects affected / exposed	3 / 339 (0.88%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	1 / 1		
PULMONARY EMBOLISM			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
PULMONARY HAEMORRHAGE			

subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
RESPIRATORY FAILURE			
subjects affected / exposed	7 / 339 (2.06%)		
occurrences causally related to treatment / all	3 / 11		
deaths causally related to treatment / all	1 / 3		
RESPIRATORY DISTRESS			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
TRACHEAL STENOSIS			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
CONFUSIONAL STATE			
subjects affected / exposed	5 / 339 (1.47%)		
occurrences causally related to treatment / all	2 / 5		
deaths causally related to treatment / all	0 / 0		
DELIRIUM			
subjects affected / exposed	2 / 339 (0.59%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
DISORIENTATION			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
MENTAL STATUS CHANGES			
subjects affected / exposed	4 / 339 (1.18%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Product issues			

Device occlusion			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
BLOOD URIC ACID INCREASED			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
EJECTION FRACTION DECREASED			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
LIVER FUNCTION TEST INCREASED			
subjects affected / exposed	2 / 339 (0.59%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
PLATELET COUNT DECREASED			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
FALL			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
FEMUR FRACTURE			

subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
HEAD INJURY			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
HUMERUS FRACTURE			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
LIGAMENT SPRAIN			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
PNEUMONITIS CHEMICAL			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	1 / 1		
TRACHEAL HAEMORRHAGE			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
ATRIAL FIBRILLATION			
subjects affected / exposed	6 / 339 (1.77%)		
occurrences causally related to treatment / all	3 / 6		
deaths causally related to treatment / all	0 / 0		
CARDIAC ARREST			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
CARDIAC FAILURE CONGESTIVE			

subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
CARDIAC TAMPONADE			
subjects affected / exposed	4 / 339 (1.18%)		
occurrences causally related to treatment / all	3 / 4		
deaths causally related to treatment / all	0 / 0		
CARDIOPULMONARY FAILURE			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
PERICARDIAL EFFUSION			
subjects affected / exposed	14 / 339 (4.13%)		
occurrences causally related to treatment / all	17 / 19		
deaths causally related to treatment / all	0 / 0		
SINUS BRADYCARDIA			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
HEMIPARESIS			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
SEIZURE			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
SPINAL CORD COMPRESSION			
subjects affected / exposed	2 / 339 (0.59%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			

ANAEMIA			
subjects affected / exposed	7 / 339 (2.06%)		
occurrences causally related to treatment / all	4 / 7		
deaths causally related to treatment / all	0 / 0		
FEBRILE NEUTROPENIA			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
THROMBOCYTOPENIA			
subjects affected / exposed	11 / 339 (3.24%)		
occurrences causally related to treatment / all	12 / 13		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	9 / 339 (2.65%)		
occurrences causally related to treatment / all	4 / 10		
deaths causally related to treatment / all	0 / 0		
ASCITES			
subjects affected / exposed	4 / 339 (1.18%)		
occurrences causally related to treatment / all	4 / 4		
deaths causally related to treatment / all	1 / 1		
COLITIS			
subjects affected / exposed	2 / 339 (0.59%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
CONSTIPATION			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
DIARRHOEA			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
GASTROINTESTINAL HAEMORRHAGE			

subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
INTESTINAL ISCHAEMIA			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
INTESTINAL OBSTRUCTION			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
NAUSEA			
subjects affected / exposed	7 / 339 (2.06%)		
occurrences causally related to treatment / all	6 / 8		
deaths causally related to treatment / all	0 / 0		
PANCREATITIS			
subjects affected / exposed	2 / 339 (0.59%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
SMALL INTESTINAL OBSTRUCTION			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
VOMITING			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
CHOLANGITIS			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
DRUG-INDUCED LIVER INJURY			

subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	1 / 1		
HEPATIC PAIN			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
HEPATOCELLULAR INJURY			
subjects affected / exposed	3 / 339 (0.88%)		
occurrences causally related to treatment / all	1 / 4		
deaths causally related to treatment / all	0 / 1		
HEPATOTOXICITY			
subjects affected / exposed	2 / 339 (0.59%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
HYPERBILIRUBINAEMIA			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
DERMATITIS EXFOLIATIVE			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
PHOTOSENSITIVITY REACTION			
subjects affected / exposed	6 / 339 (1.77%)		
occurrences causally related to treatment / all	7 / 7		
deaths causally related to treatment / all	0 / 0		
ERYTHEMA			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			

ACUTE KIDNEY INJURY			
subjects affected / exposed	3 / 339 (0.88%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
HAEMATURIA			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
RENAL FAILURE			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
RENAL IMPAIRMENT			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
BACK PAIN			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
FLANK PAIN			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
MUSCULOSKELETAL PAIN			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
MYALGIA			
subjects affected / exposed	2 / 339 (0.59%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		

RHEUMATOID ARTHRITIS			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
SPINAL PAIN			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
BACTERIAL INFECTION			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
BRONCHITIS			
subjects affected / exposed	2 / 339 (0.59%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
CELLULITIS			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
CEREBRAL TOXOPLASMOSIS			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
CLOSTRIDIUM DIFFICILE COLITIS			
subjects affected / exposed	2 / 339 (0.59%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
DEVICE RELATED INFECTION			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
DIVERTICULITIS			

subjects affected / exposed	1 / 339 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
INFECTION				
subjects affected / exposed	1 / 339 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
INFECTIVE EXACERBATION OF CHRONIC OBSTRUCTIVE AIRWAYS DISEASE				
subjects affected / exposed	1 / 339 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
LUNG INFECTION				
subjects affected / exposed	1 / 339 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
OESOPHAGEAL CANDIDIASIS				
subjects affected / exposed	1 / 339 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
PNEUMONIA				
subjects affected / exposed	12 / 339 (3.54%)			
occurrences causally related to treatment / all	2 / 16			
deaths causally related to treatment / all	0 / 1			
PULMONARY SEPSIS				
subjects affected / exposed	1 / 339 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
RESPIRATORY TRACT INFECTION				
subjects affected / exposed	3 / 339 (0.88%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 2			
SEPSIS				

subjects affected / exposed	6 / 339 (1.77%)		
occurrences causally related to treatment / all	2 / 8		
deaths causally related to treatment / all	1 / 4		
SEPTIC SHOCK			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
URINARY TRACT INFECTION			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	2 / 339 (0.59%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
DEHYDRATION			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
DIABETES MELLITUS			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
HYPOALBUMINAEMIA			
subjects affected / exposed	1 / 339 (0.29%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
HYPOKALAEMIA			
subjects affected / exposed	2 / 339 (0.59%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
HYPONATRAEMIA			

subjects affected / exposed	6 / 339 (1.77%)		
occurrences causally related to treatment / all	3 / 6		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Rovalpituzumab Tesirine		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	322 / 339 (94.99%)		
Vascular disorders			
HYPOTENSION			
subjects affected / exposed	19 / 339 (5.60%)		
occurrences (all)	21		
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	48 / 339 (14.16%)		
occurrences (all)	81		
FACE OEDEMA			
subjects affected / exposed	32 / 339 (9.44%)		
occurrences (all)	32		
FATIGUE			
subjects affected / exposed	125 / 339 (36.87%)		
occurrences (all)	170		
NON-CARDIAC CHEST PAIN			
subjects affected / exposed	19 / 339 (5.60%)		
occurrences (all)	21		
OEDEMA PERIPHERAL			
subjects affected / exposed	101 / 339 (29.79%)		
occurrences (all)	136		
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	56 / 339 (16.52%)		
occurrences (all)	67		
DYSPNOEA			

<p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>PLEURAL EFFUSION</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>83 / 339 (24.48%)</p> <p>107</p> <p>69 / 339 (20.35%)</p> <p>84</p>		
<p>Psychiatric disorders</p> <p>INSOMNIA</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>26 / 339 (7.67%)</p> <p>26</p>		
<p>Investigations</p> <p>ALANINE AMINOTRANSFERASE INCREASED</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>ASPARTATE AMINOTRANSFERASE INCREASED</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>WEIGHT DECREASED</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>20 / 339 (5.90%)</p> <p>33</p> <p>20 / 339 (5.90%)</p> <p>27</p> <p>32 / 339 (9.44%)</p> <p>36</p>		
<p>Cardiac disorders</p> <p>PERICARDIAL EFFUSION</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>38 / 339 (11.21%)</p> <p>40</p>		
<p>Nervous system disorders</p> <p>DIZZINESS</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>HEADACHE</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>33 / 339 (9.73%)</p> <p>37</p> <p>18 / 339 (5.31%)</p> <p>18</p>		
<p>Blood and lymphatic system disorders</p> <p>ANAEMIA</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>THROMBOCYTOPENIA</p>	<p>54 / 339 (15.93%)</p> <p>88</p>		

subjects affected / exposed	73 / 339 (21.53%)		
occurrences (all)	140		
Gastrointestinal disorders			
ABDOMINAL DISTENSION			
subjects affected / exposed	20 / 339 (5.90%)		
occurrences (all)	21		
ABDOMINAL PAIN			
subjects affected / exposed	42 / 339 (12.39%)		
occurrences (all)	59		
DIARRHOEA			
subjects affected / exposed	46 / 339 (13.57%)		
occurrences (all)	50		
CONSTIPATION			
subjects affected / exposed	74 / 339 (21.83%)		
occurrences (all)	87		
NAUSEA			
subjects affected / exposed	82 / 339 (24.19%)		
occurrences (all)	101		
VOMITING			
subjects affected / exposed	60 / 339 (17.70%)		
occurrences (all)	75		
Skin and subcutaneous tissue disorders			
DRY SKIN			
subjects affected / exposed	25 / 339 (7.37%)		
occurrences (all)	28		
ERYTHEMA			
subjects affected / exposed	30 / 339 (8.85%)		
occurrences (all)	37		
PHOTOSENSITIVITY REACTION			
subjects affected / exposed	119 / 339 (35.10%)		
occurrences (all)	199		
RASH			
subjects affected / exposed	26 / 339 (7.67%)		
occurrences (all)	30		
Musculoskeletal and connective tissue disorders			

<p>BACK PAIN</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>30 / 339 (8.85%)</p> <p>36</p>		
<p>MYALGIA</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>22 / 339 (6.49%)</p> <p>27</p>		
<p>Infections and infestations</p> <p>URINARY TRACT INFECTION</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>27 / 339 (7.96%)</p> <p>32</p>		
<p>Metabolism and nutrition disorders</p> <p>DECREASED APPETITE</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>DEHYDRATION</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>HYPOALBUMINAEMIA</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>HYPOKALAEMIA</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>	<p>104 / 339 (30.68%)</p> <p>124</p> <p>19 / 339 (5.60%)</p> <p>22</p> <p>54 / 339 (15.93%)</p> <p>70</p> <p>19 / 339 (5.60%)</p> <p>23</p>		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 November 2015	Allowed subjects who were deriving benefit to receive additional retreatment, beyond a total of 4 cycles, of rovalpituzumab tesirine with approval from the medical monitor; clarification of the 2 primary endpoints; update to inclusion criteria (estimated glomerular filtration rate calculation clarification and update exclusion window of other prior therapy) based on the expected half-life of agents in certain drug class; and clarification that an alternative corticosteroid could be used when dexamethasone was not available.
14 March 2016	Updates to effective birth control measures; clarification of screening window; language was added to define which hospitalizations will not be considered serious adverse events (SAEs); description of laboratory test result abnormalities and the addition of amylase and lipase to the chemistry panel.
18 November 2016	Changes were made to reflect study activities and analyses based on DLL3 IHC assays; to limit the number of enrolled 4th-line or later subjects; include efficacy analyses by line of therapy; and clarification that OS, DOR, and PFS will be based on Kaplan-Meier method, including estimates at 6, 9, and 12 months.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported