Clinical trial results:
A Phase 2, Open-Label, Single-Arm Study to Evaluate the Efficacy and Safety of Camidanlumab Tesirine (ADCT-301) in Patients with Relapsed or Refractory Hodgkin Lymphoma

Summary

EudraCT number	2018-002556-32
Trial protocol	DE BE PL FR CZ HU ES GB IT
Global end of trial date	19 January 2023

Results information

Result version number	v2 (current)
This version publication date	22 March 2024
First version publication date	01 February 2024
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	ADCT-301-201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04052997
WHO universal trial number (UTN)	-
Other trial identifiers	IND number: 121912

Notes:

Sponsors

Sponsor organisation name	ADC Therapeutics SA
Sponsor organisation address	Route de la Corniche, 3B, Epalinges, Switzerland, 1066
Public contact	Clinical Trials Information, ADC Therapeutics SA, clinicaltrials@adctherapeutics.com
Scientific contact	Clinical Trials Information, ADC Therapeutics SA, clinicaltrials@adctherapeutics.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	19 January 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 January 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluate the efficacy of single agent camidanlumab tesirine in participants with relapsed or refractory Hodgkin Lymphoma.

Protection of trial subjects:

Before initiating the study, an Investigator was required to have written and dated approval from the appropriate Institutional Review Board (IRB)/Independent Ethics Committee (IEC) for the study protocol, (i.e., a review panel responsible for ensuring the protection of the rights, safety, and well being of human participants involved in a clinical investigation, which was adequately constituted to provide assurance of that protection) according to local regulations. The IECs/IRBs were transparent in their functioning, independent of the researcher, the Sponsor, and any other undue influence, and duly qualified. All protocol amendments were reviewed and approved as required according to local regulations, prior to implementation. Other study documents subject to review during the study, including, but not limited to, serious adverse event (SAE) reports and other safety reports, were also submitted to the IEC/IRB.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 September 2019
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	3 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 6
Country: Number of subjects enrolled	United States: 50
Country: Number of subjects enrolled	Spain: 8
Country: Number of subjects enrolled	United Kingdom: 13
Country: Number of subjects enrolled	Belgium: 2
Country: Number of subjects enrolled	Czechia: 3
Country: Number of subjects enrolled	France: 5
Country: Number of subjects enrolled	Hungary: 3
Country: Number of subjects enrolled	Italy: 27
Worldwide total number of subjects	117
EEA total number of subjects	48

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)	99
From 65 to 84 years	17
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled from September 2019 to January 2023 across 9 countries (USA, Canada, Belgium, Czech Republic, France, Hungary, Italy, Spain, UK).

Pre-assignment

Screening details:

Participants with relapsed or refractory Hodgkin Lymphoma received intravenous (IV) infusions of camidanlumab tesirine.

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	Camidanlumab Tesirine

Arm description:

Participants received IV infusions of camidanlumab tesirine every 3 weeks (Q3W) at a dose of 45 µg/kg on Day 1 of each cycle (one cycle = 21 days) for 2 cycles, followed by 30 µg/kg for subsequent cycles.

Arm type	Experimental
Investigational medicinal product name	Camidanlumab Tesirine
Investigational medicinal product code	
Other name	ADCT-301
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

IV Infusion.

Number of subjects in period 1	Camidanlumab Tesirine
Started	117
Discontinued From Study	117
Completed	1
Not completed	116
Consent withdrawn by subject	17
Physician decision	50
Progression of Disease	1
Death	43
Lost to follow-up	5

Baseline characteristics

Reporting groups	
Reporting group title	Camidanlumab Tesirine
Reporting group description:	
Participants received IV infusions of camidanlumab tesirine every 3 weeks (Q3W) at a dose of 45 µg/kg on Day 1 of each cycle (one cycle = 21 days) for 2 cycles, followed by 30 µg/kg for subsequent cycles.	

Reporting group values	Camidanlumab Tesirine	Total	
Number of subjects	117	117	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	99	99	
From 65-84 years	17	17	
85 years and over	1	1	
Age continuous Units: years			
arithmetic mean	42.5		
standard deviation	± 16.24	-	
Gender categorical Units: Subjects			
Female	44	44	
Male	73	73	
Ethnicity (NIH/ OMB) Units: Subjects			
Hispanic or Latino	7	7	
Not Hispanic or Latino	104	104	
Unknown or Not Reported	6	6	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	3	3	
Native Hawaiian or Other Pacific Islander	1	1	
Black or African American	5	5	
White	101	101	
Missing	2	2	
Other	5	5	
Eastern Cooperative Oncology Group (ECOG) Performance Status Score			
The ECOG Performance Status is a scale used to assess a person's level of functioning in terms of their ability to care for themselves, daily activity, and physical ability. The scale consists of 6 grades, ranging from 0 to 5. A grade of 0 indicates the person is fully active and able to carry on as normal, and a grade			

of 5 indicates death.			
Units: Subjects			
ECOG Score 0	64	64	
ECOG Score 1	47	47	
ECOG Score 2	6	6	
ECOG Score 3	0	0	

End points

End points reporting groups

Reporting group title	Camidanlumab Tesirine

Reporting group description:

Participants received IV infusions of camidanlumab tesirine every 3 weeks (Q3W) at a dose of 45 µg/kg on Day 1 of each cycle (one cycle = 21 days) for 2 cycles, followed by 30 µg/kg for subsequent cycles.

Primary: Overall Response Rate (ORR)

End point title	Overall Response Rate (ORR)[1]

End point description:

ORR according to the 2014 Lugano classification as determined by central review in all-treated participants. ORR will be defined as the proportion of participants with a best overall response (BOR) of complete response (CR) or partial response (PR). All-Treated Population: All participants who received at least 1 dose of camidanlumab tesirine. This population was used in the primary analyses of efficacy and safety.

End point type	Primary

End point timeframe:

Up to 3 years

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: No additional statistical analyses were pre-specified for this endpoint.

End point values	Camidanlumab Tesirine			
Subject group type	Reporting group			
Number of subjects analysed	117			
Units: Count of Participants	82			

Statistical analyses

No statistical analyses for this end point

Secondary: CR Rate

End point title	CR Rate

End point description:

CR rate defined as the number of treated participants with a best overall response (BOR) of CR. All-Treated Population: All participants who received at least 1 dose of camidanlumab tesirine. This population was used in the primary analyses of efficacy and safety.

End point type	Secondary

End point timeframe:

Up to 3 years

End point values	Camidanlumab Tesirine			
Subject group type	Reporting group			
Number of subjects analysed	117			
Units: Count of Participants	39			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-Free Survival (PFS)

End point title	Progression-Free Survival (PFS)

End point description:

PFS defined as the time from first dose of study drug until the first date of either disease progression or death due to any cause. All-Treated Population: All participants who received at least 1 dose of camidanlumab tesirine. This population was used in the primary analyses of efficacy and safety.

End point type	Secondary

End point timeframe:

Up to 3 years

End point values	Camidanlumab Tesirine			
Subject group type	Reporting group			
Number of subjects analysed	117			
Units: Months				
median (confidence interval 95%)	9.13 (5.26 to 14.98)			

Statistical analyses

No statistical analyses for this end point

Secondary: Relapse-Free Survival (RFS)

End point title	Relapse-Free Survival (RFS)

End point description:

RFS defined as the time from the documentation of CR to disease progression or death. Data from participants in the All-Treated Population who achieved CR. Values of "99999" indicate the upper confidence interval was not reached due to lack of events.

End point type	Secondary

End point timeframe:

Up to 3 years

End point values	Camidanlumab Tesirine			
Subject group type	Reporting group			
Number of subjects analysed	39			
Units: Relapse-Free Survival (RFS)				
median (confidence interval 95%)	11.07 (7.36 to 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR)

End point title	Duration of Response (DOR)

End point description:

DOR defined as the time from the first documentation of tumor response to disease progression or death. Data from participants in the All-Treated Population who achieved ether CR or PR by independent reviewer.

End point type	Secondary

End point timeframe:

Up to 3 years

End point values	Camidanlumab Tesirine			
Subject group type	Reporting group			
Number of subjects analysed	82			
Units: Months				
median (confidence interval 95%)	13.73 (7.85 to 14.65)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Who Received Hematopoietic Stem Cell Transplant (HSCT)

End point title	Number of Participants Who Received Hematopoietic Stem Cell Transplant (HSCT)

End point description:

Participants receiving HSCT following camidanlumab tesirine, and without any other anticancer therapy in between, other than the therapies preparing for HSCT, were included in this analysis. All-Treated Population: All participants who received at least 1 dose of camidanlumab tesirine. This population was used in the primary analyses of efficacy and safety.

End point type	Secondary

End point timeframe:

Up to 3 years

End point values	Camidanlumab Tesirine			
Subject group type	Reporting group			
Number of subjects analysed	117			
Units: Count of Participants	18			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

OS defined as the time from first dose of study drug until death due to any cause. All-Treated Population: All participants who received at least 1 dose of camidanlumab tesirine. This population was used in the primary analyses of efficacy and safety. Values of "99999" indicate median and confidence intervals were not reached due to lack of events.

End point type	Secondary

End point timeframe:

Up to 3 years

End point values	Camidanlumab Tesirine			
Subject group type	Reporting group			
Number of subjects analysed	117			
Units: Months				
median (confidence interval 95%)	99999 (99999 to 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with ECOG Performance Status Score of 0-3 at the End of Trial (EOT)

End point title	Number of Participants with ECOG Performance Status Score of 0-3 at the End of Trial (EOT)

End point description:

The ECOG Performance Status is a scale used to asses a person's level of functioning in terms of their ability to care for themselves, daily activity, and physical ability. The scale consists of 6 grades, ranging from 0 to 5. A grade of 0 indicates the person is fully active and able to carry on as normal, and a grade of 5 indicates death. All-Treated Population: All participants who received at least 1 dose of camidanlumab tesirine and reported ECOG data at EOT. This population was used in the primary

analyses of efficacy and safety.

End point type	Secondary

End point timeframe:

EoT (up to 3 years)

End point values	Camidanlumab Tesirine			
Subject group type	Reporting group			
Number of subjects analysed	96			
Units: Count of Participants				
Score 0	43			
Score 1	37			
Score 2	12			
Score 3	4			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Who Experienced At Least One Treatment-emergent Adverse Event (TEAE)

End point title	Number of Participants Who Experienced At Least One Treatment-emergent Adverse Event (TEAE)

End point description:

An adverse event (AE) is defined as any untoward medical occurrence in a participant or clinical investigation where participants are administered a pharmaceutical product, which does not necessarily have to have a causal relationship with this treatment. A TEAE is defined as an AE that occurs or worsens in the period extending from the first dose of study drug to 30 days after the last dose of study drug in this study or start of a new anticancer therapy/procedure, whichever comes earlier. Clinically significant changes in vital signs, clinical laboratory results, and electrocardiogram were reported as AEs. All-Treated Population: All participants who received at least 1 dose of camidanlumab tesirine. This population was used in the primary analyses of efficacy and safety.

End point type	Secondary

End point timeframe:

Up to 3 years

End point values	Camidanlumab Tesirine			
Subject group type	Reporting group			
Number of subjects analysed	117			
Units: Count of Participants	116			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Who Experienced At Least One Serious Adverse Event (SAE)

End point title	Number of Participants Who Experienced At Least One Serious Adverse Event (SAE)

End point description:

An SAE is defined as any adverse event (AE) that:
• results in death
• is life threatening
• requires inpatient hospitalization or prolongation of existing hospitalization (hospitalization for elective procedures or for protocol compliance is not considered an SAE)
• results in persistent or significant disability/incapacity
• is a congenital anomaly/birth defect
• important medical events that do not meet the preceding criteria but based on appropriate medical judgement may jeopardize the participant or may require medical or surgical intervention to prevent any of the outcomes listed above.

Clinically significant changes in vital signs, clinical laboratory results, and electrocardiogram were reported as AEs. All-Treated Population: All participants who received at least 1 dose of camidanlumab tesirine. This population was used in the primary analyses of efficacy and safety.

End point type	Secondary

End point timeframe:

Up to 3 years

End point values	Camidanlumab Tesirine			
Subject group type	Reporting group			
Number of subjects analysed	117			
Units: Count of Participants	46			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Plasma Concentration (Cmax) of Camidanlumab Tesirine Total Antibody, PBD-Conjugated Antibody, and Unconjugated Warhead SG3199

End point title	Maximum Observed Plasma Concentration (Cmax) of Camidanlumab Tesirine Total Antibody, PBD-Conjugated Antibody, and Unconjugated Warhead SG3199

End point description:

PK Population: The analysis only included participants who received study drug and had at least 1 pre-Cycle 1 Day 1 and 1 post-dose valid (measurable) assessment. Due to the nature of the studied drug (antibody-drug conjugate), some PK parameters frequently could not be measured, or could be measured only briefly.

End point type	Secondary

End point timeframe:

Cycle 1 (one cycle = 21 days): day 1 (predose, EOI, 4h postdose), day 8 (168h), day 15 (336h). Cycle 2: day 1 (predose, EOI, 4h postdose), day 8 (168h), day 15 (336h)

End point values	Camidanlumab Tesirine			
Subject group type	Reporting group			
Number of subjects analysed	114			
Units: µg/L				
geometric mean (geometric coefficient of variation)				
Cycle 1 - Total Antibody	825 (± 66.7)			
Cycle 1 - Conjugated Antibody	696 (± 66.5)			
Cycle 1 - SG3199	0.0170 (± 31.6)			
Cycle 2 - Total Antibody	797 (± 62.3)			
Cycle 2 - Conjugated Antibody	685 (± 61.7)			
Cycle 2 - SG3199	0.0180 (± 38.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration-Time Curve From Time 0 to the End of the Dosing Interval (AUCtau) For Camidanlumab Tesirine Total Antibody, PBD-Conjugated Antibody, and Unconjugated Warhead SG3199

End point title	Area Under the Plasma Concentration-Time Curve From Time 0 to the End of the Dosing Interval (AUCtau) For Camidanlumab Tesirine Total Antibody, PBD-Conjugated Antibody, and Unconjugated Warhead SG3199

End point description:

PK Population: The analysis only included participants who received study drug and had at least 1 pre-Cycle 1 Day 1 and 1 post-dose valid (measurable) assessment. Due to the nature of the studied drug (antibody-drug conjugate), some PK parameters frequently could not be measured, or could be measured only briefly.

End point type	Secondary

End point timeframe:

Cycle 2 (one cycle = 21 days): day 1 (predose, EOI, 4h postdose), day 8 (168h), day 15 (336h)

End point values	Camidanlumab Tesirine			
Subject group type	Reporting group			
Number of subjects analysed	114			
Units: day*ug/L				
geometric mean (geometric coefficient of variation)				
Cycle 2 - Total Antibody	4037 (± 73.2)			
Cycle 2 - Conjugated Antibody	3067 (± 65.8)			
Cycle 2 - SG3199	0 (± 0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration-Time Curve From Time 0 to the Time of the Last Quantifiable Concentration (AUClast) For Camidanlumab Tesirine Total Antibody, PBD-Conjugated Antibody, and Unconjugated Warhead SG3199

End point title	Area Under the Plasma Concentration-Time Curve From Time 0 to the Time of the Last Quantifiable Concentration (AUClast) For Camidanlumab Tesirine Total Antibody, PBD-Conjugated Antibody, and Unconjugated Warhead SG3199

End point description:

PK Population: The analysis only included participants who received study drug and had at least 1 pre-Cycle 1 Day 1 and 1 post-dose valid (measurable) assessment. Due to the nature of the studied drug (antibody-drug conjugate), some PK parameters frequently could not be measured, or could be measured only briefly.

End point type	Secondary

End point timeframe:

Cycle 1 (one cycle = 21 days): day 1 (predose, EOI, 4h postdose), day 8 (168h), day 15 (336h). Cycle 2: day 1
(predose, EOI, 4h postdose), day 8 (168h), day 15 (336h)

End point values	Camidanlumab Tesirine			
Subject group type	Reporting group			
Number of subjects analysed	114			
Units: day*ug/L				
geometric mean (geometric coefficient of variation)				
Cycle 1 - Total Antibody	489 (± 788)			
Cycle 1 - Conjugated Antibody	345 (± 607)			
Cycle 1 - SG3199	0 (± 104)			
Cycle 2 - Total Antibody	725 (± 897)			
Cycle 2 - Conjugated Antibody	497 (± 824)			
Cycle 2 - SG3199	0 (± 211)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration-Time Curve From Time 0 to Infinity (AUCinf) For Camidanlumab Tesirine Total Antibody, PBD-Conjugated Antibody, and Unconjugated Warhead SG3199

End point title	Area Under the Plasma Concentration-Time Curve From Time 0 to Infinity (AUCinf) For Camidanlumab Tesirine Total Antibody, PBD-Conjugated Antibody, and Unconjugated Warhead SG3199

End point description:

PK Population: The analysis only included participants who received study drug and had at least 1 pre-Cycle 1 Day 1 and 1 post-dose valid (measurable) assessment. Due to the nature of the studied drug (antibody-drug conjugate), some PK parameters frequently could not be measured, or could be measured only briefly. Values of "99999" indicate that the geometric mean and coefficient of variation were not quantifiable due to the low level of observations.

End point type	Secondary

End point timeframe:

Cycle 1 (one cycle = 21 days): day 1 (predose, EOI, 4h postdose), day 8 (168h), day 15 (336h)

End point values	Camidanlumab Tesirine			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: day*µg/L				
geometric mean (geometric coefficient of variation)				
Cycle 1 - Total Antibody	6473 (± 11.9)			
Cycle 1 - Conjugated Antibody	5478 (± 31.2)			
Cycle 1 - SG3199	99999 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Clearance at Steady State (CLss) For Camidanlumab Tesirine Total Antibody, PBD-Conjugated Antibody, and Unconjugated Warhead SG3199

End point title	Clearance at Steady State (CLss) For Camidanlumab Tesirine Total Antibody, PBD-Conjugated Antibody, and Unconjugated Warhead SG3199

End point description:

PK Population: The analysis only included participants who received study drug and had at least 1 pre-Cycle 1 Day 1 and 1 post-dose valid (measurable) assessment. Due to the nature of the studied drug (antibody-drug conjugate), some PK parameters frequently could not be measured, or could be measured only briefly. Values of "99999" indicate that the geometric mean and coefficient of variation were not quantifiable due to the low level of observations.

End point type	Secondary

End point timeframe:

Cycle 2 (one cycle = 21 days): day 1 (predose, EOI, 4h postdose), day 8 (168h), day 15 (336h)

End point values	Camidanlumab Tesirine			
Subject group type	Reporting group			
Number of subjects analysed	55			
Units: L/day				
geometric mean (geometric coefficient of variation)				
Cycle 2 - Total Antibody	0.874 (± 75.6)			
Cycle 2 - Conjugated Antibody	0.958 (± 64.1)			
Cycle 2- SG3199	99999 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Clearance (CL) For Camidanlumab Tesirine Total Antibody, PBD-Conjugated Antibody, and Unconjugated Warhead SG3199

End point title	Clearance (CL) For Camidanlumab Tesirine Total Antibody, PBD-Conjugated Antibody, and Unconjugated Warhead SG3199

End point description:

PK Population: The analysis only included participants who received study drug and had at least 1 pre-Cycle 1 Day 1 and 1 post-dose valid (measurable) assessment. Due to the nature of the studied drug (antibody-drug conjugate), some PK parameters frequently could not be measured, or could be measured only briefly. Values of "99999" indicate that the geometric mean and coefficient of variation were not quantifiable due to the low level of observations.

End point type	Secondary

End point timeframe:

Cycle 1 (one cycle = 21 days): day 1 (predose, EOI, 4h postdose), day 8 (168h), day 15 (336h)

End point values	Camidanlumab Tesirine			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: L/day				
geometric mean (geometric coefficient of variation)				
Cycle 1 - Total antibody	0.556 (± 47.9)			
Cycle 1 - Conjugated Antibody	0.733 (± 34.7)			
Cycle 1 - SG3199	99999 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Apparent Terminal Elimination Half-Life (T1/2) For Camidanlumab Tesirine Total Antibody, PBD-Conjugated Antibody, and Unconjugated Warhead

SG3199	
End point title	Apparent Terminal Elimination Half-Life (T1/2) For Camidanlumab Tesirine Total Antibody, PBD-Conjugated Antibody, and Unconjugated Warhead SG3199

End point description:

PK Population: The analysis only included participants who received study drug and had at least 1 pre-Cycle 1 Day 1 and 1 post-dose valid (measurable) assessment. Due to the nature of the studied drug (antibody-drug conjugate), some PK parameters frequently could not be measured, or could be measured only briefly. Values of "99999" indicate that the geometric mean and coefficient of variation were not quantifiable due to the low level of observations.

End point type	Secondary

End point timeframe:

Cycle 1 (one cycle = 21 days): day 1 (predose, EOI, 4h postdose), day 8 (168h), day 15 (336h). Cycle 2: day 1 (predose, EOI, 4h postdose), day 8 (168h), day 15 (336h)

End point values	Camidanlumab Tesirine			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: day				
geometric mean (geometric coefficient of variation)				
Cycle 1 - Total Antibody	5.91 (± 68.6)			
Cycle 1 - Conjugated Antibody	3.89 (± 17.5)			
Cycle 1 - SG3199	99999 (± 99999)			
Cycle 2 - Total Antibody	4.46 (± 24.6)			
Cycle 2 - Conjugated Antibody	4.05 (± 26.1)			
Cycle 2 - SG3199	99999 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Volume of Distribution at Steady State (Vss) For Camidanlumab Tesirine Total Antibody, PBD-Conjugated Antibody, and Unconjugated Warhead SG3199

End point title	Volume of Distribution at Steady State (Vss) For Camidanlumab Tesirine Total Antibody, PBD-Conjugated Antibody, and Unconjugated Warhead SG3199

End point description:

PK Population: The analysis only included participants who received study drug and had at least 1 pre-Cycle 1 Day 1 and 1 post-dose valid (measurable) assessment. Due to the nature of the studied drug (antibody-drug conjugate), some PK parameters frequently could not be measured, or could be measured only briefly. Values of "99999" indicate that the geometric mean and coefficient of variation were not quantifiable due to the low level of observations.

End point type	Secondary

End point timeframe:

Cycle 1 (one cycle = 21 days): day 1 (predose, EOI, 4h postdose), day 8 (168h), day 15 (336h). Cycle 2: day 1 (predose, EOI, 4h postdose), day 8 (168h), day 15 (336h)

End point values	Camidanlumab Tesirine			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: Liters				
geometric mean (geometric coefficient of variation)				
Cycle 1 - Total Antibody	5.91 (± 68.6)			
Cycle 1 - Conjugated Antibody	2.81 (± 24.9)			
Cycle 1 - SG3199	99999 (± 99999)			
Cycle 2 - Total Antibody	3.14 (± 44.1)			
Cycle 2 - Conjugated Antibody	3.17 (± 37.6)			
Cycle 2 - SG3199	99999 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Accumulation Index (AI) For Camidanlumab Tesirine Total Antibody, PBD-Conjugated Antibody, and Unconjugated Warhead SG3199

End point title	Accumulation Index (AI) For Camidanlumab Tesirine Total Antibody, PBD-Conjugated Antibody, and Unconjugated Warhead SG3199

End point description:

AI is the ratio of area under the serum concentration-time curve (AUC) from 0 to 21 days for Cycle 2 divided by AUC from 0 to 21 days for Cycle 1. PK Population: The analysis only included participants who received study drug and had at least 1 pre-Cycle 1 Day 1 and 1 post-dose valid (measurable) assessment. Due to the nature of the studied drug (antibody-drug conjugate), some PK parameters frequently could not be measured, or could be measured only briefly. Values of "99999" indicate that the geometric mean and coefficient of variation were not quantifiable due to the low level of observations.

End point type	Secondary

End point timeframe:

Cycle 1 and 2: day 0 to 21

End point values	Camidanlumab Tesirine			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: Ratio				
geometric mean (geometric coefficient of variation)				
Total Antibody	1.30 (± 52.9)			
Conjugated Antibody	1.04 (± 4.00)			
SG3199	99999 (± 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Confirmed Positive Anti-Drug Antibody (ADA) Responses Post Dose

End point title	Number of Participants With Confirmed Positive Anti-Drug Antibody (ADA) Responses Post Dose

End point description:

Detection of ADAs was performed by using a screening assay for identification of antibody positive samples/participants, a confirmation assay, and titer assessment. All-Treated Population: All participants who received at least 1 dose of camidanlumab tesirine. This population was used in the primary analyses of efficacy and safety.

End point type	Secondary

End point timeframe:

Up to 3 years

End point values	Camidanlumab Tesirine			
Subject group type	Reporting group			
Number of subjects analysed	117			
Units: Count of Participants	2			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Health-Related Quality of Life (HRQoL) as Measured by EuroQoL-5 Dimensions-5 Levels (EQ-5D-5L) Visual Analog Scale (VAS)

End point title	Change From Baseline in Health-Related Quality of Life (HRQoL) as Measured by EuroQoL-5 Dimensions-5 Levels (EQ-5D-5L) Visual Analog Scale (VAS)

End point description:

Participants were asked to indicate their health state on a VAS with scores ranging from ‘the worst health you can imagine’ (score 0) to 'the best health you can imagine’ (score 100). Participants are asked to mark an “X” on the VAS to indicate their own health and then to report the score in a text box. Positive changes from Baseline represent an an improvement in heath. Patient Reported Outcome (PRO) Population: All participants in the all-treated patients with baseline score (at least one instrument) and at least 1 post-baseline score (in at least one instrument).

End point type	Secondary

End point timeframe:

Baseline, Day 1 of Cycles 2 to 15 (one cycle = 21 days) and EOT (up to 3 years)

End point values	Camidanlumab Tesirine			
Subject group type	Reporting group			
Number of subjects analysed	116			
Units: Score on a scale				
arithmetic mean (standard deviation)				
Cycle 2 (n = 111)	3.6 (± 14.41)			
Cycle 3 (n = 90)	5.2 (± 15.14)			
Cycle 4 (n = 74)	4.9 (± 17.65)			
Cycle 5 (n = 62)	4.6 (± 19.66)			
Cycle 6 (n = 44)	-1.2 (± 14.97)			
Cycle 7 (n = 32)	4.5 (± 11.88)			
Cycle 8 (n = 19)	4.5 (± 13.24)			
Cycle 9 (n = 17)	3.3 (± 13.74)			
Cycle 10 (n = 11)	1.3 (± 7.30)			
Cycle 11 (n = 7)	-0.6 (± 10.44)			
Cycle 12 (n = 6)	-4.8 (± 5.31)			
Cycle 13 (n = 3)	-1.7 (± 2.89)			
Cycle 14 (n = 3)	-1.7 (± 10.41)			
Cycle 15 (n = 3)	-3.3 (± 7.64)			
EOT (n = 80)	-3.1 (± 20.06)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in HRQoL as Measured by Functional Assessment of Cancer Therapy - Lymphoma (FACT-Lym)

End point title	Change From Baseline in HRQoL as Measured by Functional Assessment of Cancer Therapy - Lymphoma (FACT-Lym)

End point description:

The FACT-Lym consists of a 27-item general core questionnaire (i.e., Functional Assessment of Cancer Therapy - General [FACT-G]) and a 15-item disease-specific questionnaire (Lymphoma Subscale). The FACT-G includes 4 domains: physical well-being, social/family well-being, emotional well-being, and functional well-being. The total FACT Lym score (0-168) was obtained by summing individual subscale scores. Higher scores for the scales indicate better quality of life. Change was calculated as the value at the last observation minus the value at baseline. PRO Population: All participants in the all-treated patients with baseline score (at least one instrument) and at least 1 post-baseline score (in at least one instrument).

End point type	Secondary

End point timeframe:

Baseline, Day 1 of Cycles 2 to 15 (one cycle = 21 days) and EOT (up to 3 years)

End point values	Camidanlumab Tesirine			
Subject group type	Reporting group			
Number of subjects analysed	116			
Units: Score on a scale				
arithmetic mean (standard deviation)				
Cycle 2 (n = 108)	-0.45 (± 4.079)			
Cycle 3 (n = 89)	-0.02 (± 4.935)			
Cycle 4 (n = 73)	-0.20 (± 5.384)			
Cycle 5 (n = 57)	-0.13 (± 4.906)			
Cycle 6 (n = 42)	-1.29 (± 4.318)			
Cycle 7 (n = 30)	0.39 (± 3.892)			
Cycle 8 (n = 19)	0.40 (± 4.419)			
Cycle 9 (n = 17)	-1.38 (± 6.262)			
Cycle 10 (n = 10)	1.16 (± 2.374)			
Cycle 11 (n = 6)	1.50 (± 5.167)			
Cycle 12 (n = 5)	-1.40 (± 0.548)			
Cycle 13 (n = 2)	0.00 (± 0.000)			
Cycle 14 (n = 2)	0.00 (± 0.000)			
Cycle 15 (n = 2)	0.00 (± 0.000)			
EOT (n = 77)	-3.06 (± 6.802)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 3 years

Adverse event reporting additional description:

All AEs, AESIs, and SAEs regardless of relationship to study drug were reported from the time a participant signed the ICF until 30 days after the last dose of study drug. After 30 days following the last dose of study drug, only related SAEs were reported.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.0.

Reporting groups

Reporting group title	Camidanlumab Tesirine

Reporting group description:

All participants received IV infusions of camidanlumab tesirine Q3W at a dose of 45 µg/kg on Day 1 of each cycle (one cycle = 21 days) for 2 cycles, followed by 30 µg/kg for subsequent cycles.

Serious adverse events	Camidanlumab Tesirine		
Total subjects affected by serious adverse events			
subjects affected / exposed	46 / 117 (39.32%)		
number of deaths (all causes)	3		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	1 / 117 (0.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Superior vena cava occlusion			
subjects affected / exposed	1 / 117 (0.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Shock haemorrhagic			
subjects affected / exposed	1 / 117 (0.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			

Pyrexia			
subjects affected / exposed	3 / 117 (2.56%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pneumonitis			
subjects affected / exposed	2 / 117 (1.71%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Respiratory failure			
subjects affected / exposed	1 / 117 (0.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Dyspnoea			
subjects affected / exposed	1 / 117 (0.85%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Acute respiratory failure			
subjects affected / exposed	1 / 117 (0.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Product issues			
Device occlusion			
subjects affected / exposed	1 / 117 (0.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Transplant failure			
subjects affected / exposed	1 / 117 (0.85%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Left ventricular failure			

subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Acute myocardial infarction				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Cardiac arrest				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Nervous system disorders				
Radiculopathy				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Peripheral sensory neuropathy				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Peripheral motor neuropathy				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Epilepsy				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Guillain-Barre syndrome				

subjects affected / exposed	4 / 117 (3.42%)			
occurrences causally related to treatment / all	4 / 4			
deaths causally related to treatment / all	0 / 0			
Syncope				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Bone marrow failure				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Febrile neutropenia				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Duodenal ulcer				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Inguinal hernia				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intestinal obstruction				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	2 / 117 (1.71%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Duodenal ulcer perforation				

subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Small intestinal obstruction				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Drug-induced liver injury				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Photosensitivity reaction				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Parakeratosis				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Lichenoid keratosis				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Dermatosis				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Eczema				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Rash maculo-papular				

subjects affected / exposed	3 / 117 (2.56%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Dermatitis exfoliative generalised			
subjects affected / exposed	1 / 117 (0.85%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Tubulointerstitial nephritis			
subjects affected / exposed	1 / 117 (0.85%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Acute kidney injury			
subjects affected / exposed	1 / 117 (0.85%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Thyroiditis			
subjects affected / exposed	1 / 117 (0.85%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Muscular weakness			
subjects affected / exposed	1 / 117 (0.85%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Myositis			
subjects affected / exposed	1 / 117 (0.85%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia pneumococcal			

subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	2 / 117 (1.71%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Adenovirus infection				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bronchopulmonary aspergillosis				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
JC virus infection				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Septic shock				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia bacterial				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Rash pustular				

subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Tooth infection				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Varicella zoster virus infection				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	2 / 117 (1.71%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Lung infection				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Diabetic ketoacidosis				
subjects affected / exposed	2 / 117 (1.71%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Acidosis				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Dehydration				
subjects affected / exposed	1 / 117 (0.85%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Electrolyte imbalance				

subjects affected / exposed	1 / 117 (0.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hyperglycaemia			
subjects affected / exposed	1 / 117 (0.85%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Type 1 diabetes mellitus			
subjects affected / exposed	1 / 117 (0.85%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Camidanlumab Tesirine		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	112 / 117 (95.73%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	6 / 117 (5.13%)		
occurrences (all)	9		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	34 / 117 (29.06%)		
occurrences (all)	47		
Oedema peripheral			
subjects affected / exposed	14 / 117 (11.97%)		
occurrences (all)	15		
Face oedema			
subjects affected / exposed	7 / 117 (5.98%)		
occurrences (all)	7		
Chills			
subjects affected / exposed	12 / 117 (10.26%)		
occurrences (all)	14		
Asthenia			

subjects affected / exposed	8 / 117 (6.84%)		
occurrences (all)	8		
Fatigue			
subjects affected / exposed	45 / 117 (38.46%)		
occurrences (all)	53		
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	10 / 117 (8.55%)		
occurrences (all)	11		
Dyspnoea			
subjects affected / exposed	16 / 117 (13.68%)		
occurrences (all)	18		
Cough			
subjects affected / exposed	12 / 117 (10.26%)		
occurrences (all)	12		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	16 / 117 (13.68%)		
occurrences (all)	17		
Anxiety			
subjects affected / exposed	6 / 117 (5.13%)		
occurrences (all)	8		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	15 / 117 (12.82%)		
occurrences (all)	16		
Amylase increased			
subjects affected / exposed	9 / 117 (7.69%)		
occurrences (all)	12		
Gamma-glutamyltransferase increased			
subjects affected / exposed	20 / 117 (17.09%)		
occurrences (all)	26		
Aspartate aminotransferase increased			
subjects affected / exposed	14 / 117 (11.97%)		
occurrences (all)	17		

Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	11 / 117 (9.40%) 15		
Lipase increased subjects affected / exposed occurrences (all)	9 / 117 (7.69%) 11		
Weight decreased subjects affected / exposed occurrences (all)	9 / 117 (7.69%) 9		
Cardiac disorders Sinus tachycardia subjects affected / exposed occurrences (all)	8 / 117 (6.84%) 8		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	19 / 117 (16.24%) 22		
Dysgeusia subjects affected / exposed occurrences (all)	6 / 117 (5.13%) 6		
Dizziness subjects affected / exposed occurrences (all)	12 / 117 (10.26%) 13		
Neuropathy peripheral subjects affected / exposed occurrences (all)	6 / 117 (5.13%) 6		
Peripheral sensory neuropathy subjects affected / exposed occurrences (all)	7 / 117 (5.98%) 7		
Blood and lymphatic system disorders Lymphopenia subjects affected / exposed occurrences (all)	18 / 117 (15.38%) 26		
Neutropenia subjects affected / exposed occurrences (all)	19 / 117 (16.24%) 29		
Thrombocytopenia			

subjects affected / exposed	24 / 117 (20.51%)		
occurrences (all)	34		
Anaemia			
subjects affected / exposed	29 / 117 (24.79%)		
occurrences (all)	39		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	19 / 117 (16.24%)		
occurrences (all)	26		
Dry mouth			
subjects affected / exposed	7 / 117 (5.98%)		
occurrences (all)	7		
Stomatitis			
subjects affected / exposed	6 / 117 (5.13%)		
occurrences (all)	6		
Nausea			
subjects affected / exposed	32 / 117 (27.35%)		
occurrences (all)	40		
Dyspepsia			
subjects affected / exposed	6 / 117 (5.13%)		
occurrences (all)	6		
Constipation			
subjects affected / exposed	20 / 117 (17.09%)		
occurrences (all)	23		
Abdominal pain			
subjects affected / exposed	12 / 117 (10.26%)		
occurrences (all)	14		
Vomiting			
subjects affected / exposed	13 / 117 (11.11%)		
occurrences (all)	17		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	31 / 117 (26.50%)		
occurrences (all)	36		
Rash maculo-papular			

subjects affected / exposed occurrences (all)	38 / 117 (32.48%) 46		
Erythema subjects affected / exposed occurrences (all)	14 / 117 (11.97%) 19		
Dry skin subjects affected / exposed occurrences (all)	7 / 117 (5.98%) 8		
Pruritus subjects affected / exposed occurrences (all)	28 / 117 (23.93%) 30		
Endocrine disorders			
Hyperthyroidism subjects affected / exposed occurrences (all)	8 / 117 (6.84%) 8		
Hypothyroidism subjects affected / exposed occurrences (all)	12 / 117 (10.26%) 12		
Thyroiditis subjects affected / exposed occurrences (all)	6 / 117 (5.13%) 6		
Musculoskeletal and connective tissue disorders			
Arthralgia subjects affected / exposed occurrences (all)	19 / 117 (16.24%) 22		
Pain in extremity subjects affected / exposed occurrences (all)	6 / 117 (5.13%) 9		
Myalgia subjects affected / exposed occurrences (all)	11 / 117 (9.40%) 15		
Infections and infestations			
Upper respiratory tract infection subjects affected / exposed occurrences (all)	7 / 117 (5.98%) 8		
Metabolism and nutrition disorders			

Hyperglycaemia			
subjects affected / exposed	14 / 117 (11.97%)		
occurrences (all)	21		
Dehydration			
subjects affected / exposed	6 / 117 (5.13%)		
occurrences (all)	7		
Decreased appetite			
subjects affected / exposed	12 / 117 (10.26%)		
occurrences (all)	12		
Hypokalaemia			
subjects affected / exposed	14 / 117 (11.97%)		
occurrences (all)	18		
Hypomagnesaemia			
subjects affected / exposed	9 / 117 (7.69%)		
occurrences (all)	10		
Hyponatraemia			
subjects affected / exposed	7 / 117 (5.98%)		
occurrences (all)	9		
Hypophosphataemia			
subjects affected / exposed	21 / 117 (17.95%)		
occurrences (all)	29		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 June 2019	The primary reason for Protocol Amendment 1 was to include changes based on recommendations by the United States (US) Food and Drug Administration (FDA). In addition, substantial updates in line with study needs had been introduced, e.g., revision of study drug instructions or clarifications of male participant contraception methods.
24 April 2020	The primary reason for this global Protocol Amendment 2 was to combine the updates required by the Regulatory Authorities and IRB/IEC received to date in one global protocol version. In addition, updates in line with study needs had been introduced, such as the inclusion of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) added to the list of pathogens associated to Guillain-Barré syndrome (GBS), additional recommendation to capture early signs of polyradiculopathy/GBS, and the update of the study stopping rule.
01 July 2020	The primary reason for this global Protocol Amendment 3 was to update the stopping rule and to exclude participants that are tested positive for influenza and SARS-CoV-2 before initiating study treatment, based on the recommendations by the FDA.
06 November 2020	The primary reasons for this global Protocol Amendment 4 were to implement the recommendations from the independent Data and Safety Monitoring Board (iDSMB), including the addition of varicella zoster virus prophylaxis, an update of the management guidance in respect to specific autoimmune toxicities, and to address the requests from the French and Belgian regulatory authorities.
16 February 2022	The primary reason for Protocol Amendment 5 is to extend the contraception period after last dose of camidanlumab tesirine, following an urgent safety measure. The contraception period is determined based on the compound properties and half-life, and has been updated due to a recently revised half-life value of camidanlumab tesirine.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date

17 April 2020	The US FDA placed the trial ADCT-301-201 on a partial clinical hold following 2 cases of GBS/polyradiculopathy. An ad hoc iDSMB meeting to perform comprehensive safety evaluation was held on 15 Apr 2020 (recommendations issued: accrual can continue; create a stopping rule that rules out a probability of ≥ 20% of GBS). ADCT applied the conditions set out by the US FDA in the partial clinical hold to all investigator sites. Under the partial clinical hold, no new participants were treated with camidanlumab tesirine. All ongoing participants at the time of the clinical hold were informed and consented to continue, with the following specifications: Ongoing participants who were deriving clinical benefit (includes participants with an objective response and stable disease) were permitted to continue treatment per protocol if they chose after being re-consented. In the EU, all countries were notified about the clinical hold in mid Apr 2020. The clinical hold was subsequently lifted in the EU countries in Aug-Oct 2020.	02 July 2020

Notes:

Limitations and caveats

None reported