



Clinical trial results:

A Phase 2, Multicenter, Open-Label Study of Tislelizumab (BGB-A317) in Patients With Relapsed or Refractory Classical Hodgkin Lymphoma

Summary

EudraCT number	2019-002105-22
Trial protocol	FR ES IT
Global end of trial date	29 August 2024

Results information

Result version number	v1
This version publication date	10 September 2025
First version publication date	10 September 2025

Trial information

Trial identification

Sponsor protocol code	BGB-A317-210
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04318080
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	BeiGene, Ltd., c/o BeiGene USA, Inc.
Sponsor organisation address	311 Pennington-Rocky Hill Rd, Pennington, NJ, United States, 08534
Public contact	BeiGene Clinical Support, BeiGene USA, Inc., 1 877-828-5568, clinicaltrials@beigene.com
Scientific contact	BeiGene Clinical Support, BeiGene USA, Inc., 1 877-828-5568, clinicaltrials@beigene.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	29 August 2024
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	29 August 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This was a Phase 2 trial evaluating the effectiveness and safety of tislelizumab in participants with relapsed or hard-to-treat classical Hodgkin lymphoma (cHL). Participants were grouped by prior treatments. The main outcome was to assess overall response rate (ORR) across both cohorts. Participants continued receiving the study treatment until their disease got worse, side effects became too severe, or they chose to stop for other reasons.

Protection of trial subjects:

This study was conducted in accordance with sponsor procedures, which comply with the principles of Good Clinical Practice (GCP), International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use Guidelines, the Declaration of Helsinki, and applicable local regulatory requirements.

The protocol, any amendments, and informed consent forms were reviewed and approved by the Independent Ethics Committee/Institutional Review Board in conformance with GCP and applicable regulatory requirements.

Before a patient was enrolled in the study, he or she was provided with a written informed consent form that complied with GCP. The investigator (or designee) explained to each patient the nature of the study, its purpose, procedures, expected duration, and the benefits and risks involved with study participation. Patients were given the opportunity to ask questions and were informed of their right to withdraw from the study at any time without prejudice. Informed consent was obtained before any screening or study-specific procedures were performed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 August 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 2
Country: Number of subjects enrolled	Belgium: 3
Country: Number of subjects enrolled	France: 38
Country: Number of subjects enrolled	United States: 3
Worldwide total number of subjects	46
EEA total number of subjects	41

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)	25
From 65 to 84 years	18
85 years and over	3

Subject disposition

Recruitment

Recruitment details:

This study was conducted at multiple centers across France, the United States, Belgium, and Australia from August 20, 2020, to August 29, 2024.

Pre-assignment

Screening details:

Treatment started within 14 days of eligibility confirmation, within the screening window. Treatment continued until disease progression, unacceptable toxicity, or withdrawal. Participants who did not meet eligibility criteria during screening were excluded prior to assignment to treatment groups.

Period 1

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

Arms

Are arms mutually exclusive?	No
Arm title	Cohort 1

Arm description:

Participants who had relapsed or refractory classical Hodgkin lymphoma and had either not achieved a response or had disease progression following autologous hematopoietic stem cell transplantation received tislelizumab 200 milligrams (mg) intravenously every 3 weeks.

Arm type	Experimental
Investigational medicinal product name	Tislelizumab
Investigational medicinal product code	BGB-A317
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Tislelizumab: 200 milligrams (mg) intravenously every 3 weeks (Q3W)

Arm title	Cohort 2
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Arm description:

Participants who had relapsed or refractory classical Hodgkin lymphoma and had either not achieved a response or had disease progression after at least one prior systemic therapy and were not candidates for autologous or allogeneic hematopoietic stem cell transplantation received tislelizumab 200 mg intravenously every 3 weeks.

Arm type	Experimental
Investigational medicinal product name	Tislelizumab
Investigational medicinal product code	BGB-A317
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Tislelizumab: 200 milligrams (mg) intravenously every 3 weeks (Q3W)

Arm title	Total
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Arm description:

Participants received tislelizumab 200 mg intravenously every 3 weeks.

Arm type	Experimental
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Investigational medicinal product name	Tislelizumab
Investigational medicinal product code	BGB-A317
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Tislelizumab: 200 miligrams (mg) intravenously every 3 weeks (Q3W)

Number of subjects in period 1	Cohort 1	Cohort 2	Total
Started	15	31	46
Treated	14	31	45
Completed	0	0	0
Not completed	15	31	46
Consent withdrawn by subject	1	-	1
Protocol Deviation	1	-	1
Death	3	9	12
Study Completed by Sponsor	10	22	32

Baseline characteristics

Reporting groups

Reporting group title	Cohort 1
Reporting group description: Participants who had relapsed or refractory classical Hodgkin lymphoma and had either not achieved a response or had disease progression following autologous hematopoietic stem cell transplantation received tislelizumab 200 milligrams (mg) intravenously every 3 weeks.	
Reporting group title	Cohort 2
Reporting group description: Participants who had relapsed or refractory classical Hodgkin lymphoma and had either not achieved a response or had disease progression after at least one prior systemic therapy and were not candidates for autologous or allogeneic hematopoietic stem cell transplantation received tislelizumab 200 mg intravenously every 3 weeks.	
Reporting group title	Total
Reporting group description: Participants received tislelizumab 200 mg intravenously every 3 weeks.	

Reporting group values	Cohort 1	Cohort 2	Total
Number of subjects	15	31	46
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
arithmetic mean	43.9	59.6	54.7
standard deviation	± 15.78	± 21.95	± 21.37
Gender categorical Units: Subjects			
Female	4	11	15
Male	10	20	30
Not recorded	1	0	1
Patient Status at Time of Enrollment			
Refractory refers to participants whose disease did not respond to their most recent prior therapy (no complete or partial response). Relapse or Progression refers to participants whose disease initially responded to prior therapy but later worsened, progressed, or returned. One participant in Cohort 1 was enrolled but did not receive study drug due to screen failure. This participant is included in the baseline characteristics to meet EudraCT reporting requirements, but was not included in the efficacy or safety analyses.			
Units: Subjects			
Refractory	0	13	13
Relapse or Progression	14	18	32

Unknown	1	0	1
Number of prior lines of therapy for cHL			
One participant in Cohort 1 was enrolled but did not receive study drug due to screen failure. This participant is included in the baseline characteristics to meet EudraCT reporting requirements, but was not included in the efficacy or safety analyses.			
Units: Subjects			
One	0	7	7
Two	9	17	26
Three	4	6	10
Four	1	1	2
Not Collected	1	0	1
Eastern Cooperative Oncology Group Performance Status			
Eastern Cooperative Oncology Group Performance Status is a standard scale used to assess how a participant's disease impacts their daily living abilities. Zero refers to normal activities. One is ambulatory able to carry out work. One participant in Cohort 1 was enrolled but did not receive study drug due to screen failure. This participant is included in the baseline characteristics to meet EudraCT reporting requirements, but was not included in the efficacy or safety analyses.			
Units: Subjects			
Zero	10	18	28
One	4	13	17
Not Collected	1	0	1
Race (customized)			
Units: Subjects			
White	3	5	8
Not collected	12	26	38

Reporting group values	Total		
Number of subjects	46		
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	15		
Male	30		
Not recorded	1		
Patient Status at Time of Enrollment			
Refractory refers to participants whose disease did not respond to their most recent prior therapy (no complete or partial response). Relapse or Progression refers to participants whose disease initially			

responded to prior therapy but later worsened, progressed, or returned. One participant in Cohort 1 was enrolled but did not receive study drug due to screen failure. This participant is included in the baseline characteristics to meet EudraCT reporting requirements, but was not included in the efficacy or safety analyses.

Units: Subjects			
Refractory	13		
Relapse or Progression	32		
Unknown	1		

Number of prior lines of therapy for cHL			
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One participant in Cohort 1 was enrolled but did not receive study drug due to screen failure. This participant is included in the baseline characteristics to meet EudraCT reporting requirements, but was not included in the efficacy or safety analyses.

Units: Subjects			
One	7		
Two	26		
Three	10		
Four	2		
Not Collected	1		

Eastern Cooperative Oncology Group Performance Status			
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Eastern Cooperative Oncology Group Performance Status is a standard scale used to assess how a participant's disease impacts their daily living abilities. Zero refers to normal activities. One is ambulatory able to carry out work. One participant in Cohort 1 was enrolled but did not receive study drug due to screen failure. This participant is included in the baseline characteristics to meet EudraCT reporting requirements, but was not included in the efficacy or safety analyses.

Units: Subjects			
Zero	28		
One	17		
Not Collected	1		

Race (customized)			
Units: Subjects			
White	8		
Not collected	38		

End points

End points reporting groups

Reporting group title	Cohort 1
Reporting group description: Participants who had relapsed or refractory classical Hodgkin lymphoma and had either not achieved a response or had disease progression following autologous hematopoietic stem cell transplantation received tislelizumab 200 milligrams (mg) intravenously every 3 weeks.	
Reporting group title	Cohort 2
Reporting group description: Participants who had relapsed or refractory classical Hodgkin lymphoma and had either not achieved a response or had disease progression after at least one prior systemic therapy and were not candidates for autologous or allogeneic hematopoietic stem cell transplantation received tislelizumab 200 mg intravenously every 3 weeks.	
Reporting group title	Total
Reporting group description: Participants received tislelizumab 200 mg intravenously every 3 weeks.	

Primary: Overall Response Rate (ORR)

End point title	Overall Response Rate (ORR)
End point description: ORR was defined as the percentage of participants who achieved a best overall response of complete response (CR) or partial response (PR) by Positron Emission Tomography (PET) and Computed Tomography (CT) per the Lugano Classification and as determined by the investigator. CR was defined as the complete disappearance of all target lesions on PET-CT, with no new lesions detected. PR was defined as a significant reduction in metabolic activity or lesion size consistent with partial tumor shrinkage as per Lugano criteria.	
End point type	Primary
End point timeframe: From first dose to primary analysis data cutoff (12 Dec 2022) or new anti-lymphoma therapy start, whichever came first. Median follow-up was 11.4 months.	

End point values	Cohort 1	Cohort 2	Total	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14	31	45	
Units: Percentage of Participants				
number (confidence interval 95%)	64.3 (35.1 to 87.2)	64.5 (45.4 to 80.8)	64.4 (48.8 to 78.1)	

Statistical analyses

Statistical analysis title	ORR
Statistical analysis description: The primary analysis was conducted on both cohorts combined, A binomial exact test was performed to test the null hypothesis (H0: ORR = 45% based on previous clinical trials) and alternative hypothesis (ORR >45%). If the one-sided p-value was ≤ 0.05, tislelizumab was considered to statistically significantly increase ORR compared to the historical control.	

Comparison groups	Total v Cohort 2 v Cohort 1
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority ^[1]
P-value	= 0.0044 ^[2]
Method	Binomial Exact Test

Notes:

[1] - Analysis tested whether ORR with tislelizumab was superior to a historical ORR of 45% using a one-sided binomial exact test ($\alpha = 0.05$).

[2] - One-sided p-value based on a binomial exact test comparing observed ORR to historical rate of 45%.

Secondary: Complete Response Rate (CRR)

End point title	Complete Response Rate (CRR)
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End point description:

CRR was defined as the percentage of participants who achieved a best overall response of complete response (CR) by PET-CT or CT per the Lugano Classification and determined by the investigator. CR was defined as the complete disappearance of all target lesions on PET-CT or CT, with no new lesions detected.

End point type	Secondary
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End point timeframe:

From first dose to primary analysis data cutoff (12 Dec 2022) or new anti-lymphoma therapy start, whichever came first. Median follow-up was 11.4 months.

End point values	Cohort 1	Cohort 2	Total	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	14	31	45	
Units: Percentage of Participants				
number (confidence interval 95%)	42.9 (17.7 to 71.1)	25.8 (11.9 to 44.6)	31.1 (18.2 to 46.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR)

End point title	Duration of Response (DOR)
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End point description:

DOR was defined as the time from the date that response criteria (CR or PR) were first met to the date of objectively documented disease progression or death, whichever occurred first. Participants without an event were censored at the data cutoff or end of study, whichever occurred first. Participants who received new anti-lymphoma therapies, including Hematopoietic Stem Cell Transplantation (HSCT), before having an event were censored at the date of therapy initiation. Only participants with confirmed response were included in the analysis. Median DOR was estimated using the Kaplan-Meier method.

The responder analysis set only included participants with a confirmed response (CR) or partial response (PR).

End point type	Secondary
End point timeframe:	
From first dose to primary analysis data cutoff (12 Dec 2022) or new anti-lymphoma therapy start, whichever came first. Median follow-up was 11.4 months.	

End point values	Cohort 1	Cohort 2	Total	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	20	29	
Units: Months				
median (confidence interval 95%)	12.25 (5.55 to 12.25)	6.64 (2.79 to 9999)	12.25 (3.02 to 9999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Response (TTR)

End point title	Time to Response (TTR)
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End point description:

TTR was defined as the time from the date of the first dose of tislelizumab to the date the response criteria were first met CR or PR per the Lugano Classification, and was analyzed only in participants who achieved an overall response; CR was defined as complete disappearance of disease, PR as $\geq 50\%$ reduction in tumor burden, and Overall Response Rate (ORR) included participants with either CR or PR. Median TTR was estimated using the Kaplan-Meier method.

Safety Analysis Set. Only participants who had achieved an overall response were included in the analysis of time to response.

End point type	Secondary
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End point timeframe:

From first dose to primary analysis data cutoff (12 Dec 2022) or new anti-lymphoma therapy start, whichever came first. Median follow-up was 11.4 months.

End point values	Cohort 1	Cohort 2	Total	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	20	29	
Units: Months				
median (confidence interval 95%)	2.69 (2.1 to 5.5)	2.69 (0.3 to 5.6)	2.69 (0.3 to 5.6)	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Experiencing Treatment-Emergent Adverse Events (TEAEs) and Serious Adverse Events (SAEs)

End point title	Number of Participants Experiencing Treatment-Emergent Adverse Events (TEAEs) and Serious Adverse Events (SAEs) ^[3]
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End point description:

Adverse events (AEs) were assessed according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI-CTCAE) Version 5.0. Treatment-emergent adverse events (TEAEs) were defined as any AE that began or worsened in severity after the first dose of study treatment and up to 90 days following the last dose, regardless of initiation of new anti-lymphoma therapy. The following safety data are reported:

Number of participants with any TEAEs: Participants who experienced at least one TEAE of any grade.

Number of participants with any Grade ≥ 3 TEAEs: Participants who experienced at least one TEAE that was Grade 3 or higher in severity.

Number of participants with any SAEs: Participants who experienced at least one serious adverse event, regardless of relationship to study treatment, occurring up to 90 days after the last dose.

End point type	Secondary
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End point timeframe:

From the date of the first dose of tislelizumab through 90 days after the last dose (maximum duration of tislelizumab exposure was 168 weeks)

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The third arm in the baseline period is labeled as Total to show the totals for efficacy endpoints. It does not pertain to safety analysis and cannot be reported on.

End point values	Cohort 1	Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	14	31		
Units: Participants				
Number of participants with any TEAEs	12	30		
Number of participants with any TEAEs with grade >	4	12		
Number of participants with any SAEs	4	9		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All-cause mortality was reported from randomization to 29 Aug 2024 (4 years). AEs were reported from first tislelizumab dose to 90 days post-last dose (max exposure: 168 weeks).

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	27

Reporting groups

Reporting group title	Cohort 2
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Reporting group description:

Cohort 2

Reporting group title	Cohort 1
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Reporting group description:

Cohort 1

Serious adverse events	Cohort 2	Cohort 1	
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 31 (29.03%)	4 / 14 (28.57%)	
number of deaths (all causes)	9	3	
number of deaths resulting from adverse events	1	0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 31 (3.23%)	0 / 14 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 31 (0.00%)	1 / 14 (7.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lipase increased			
subjects affected / exposed	0 / 31 (0.00%)	1 / 14 (7.14%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Troponin increased			

subjects affected / exposed	1 / 31 (3.23%)	0 / 14 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 31 (3.23%)	0 / 14 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cutaneous t-cell lymphoma			
subjects affected / exposed	0 / 31 (0.00%)	1 / 14 (7.14%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	1 / 31 (3.23%)	0 / 14 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			
subjects affected / exposed	1 / 31 (3.23%)	0 / 14 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	1 / 31 (3.23%)	0 / 14 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 31 (3.23%)	0 / 14 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Coeliac disease			

subjects affected / exposed	1 / 31 (3.23%)	0 / 14 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 31 (0.00%)	1 / 14 (7.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Skin ulcer			
subjects affected / exposed	1 / 31 (3.23%)	0 / 14 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Musculoskeletal chest pain			
subjects affected / exposed	0 / 31 (0.00%)	1 / 14 (7.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polyarthritis			
subjects affected / exposed	1 / 31 (3.23%)	0 / 14 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Sepsis			
subjects affected / exposed	1 / 31 (3.23%)	0 / 14 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	1 / 31 (3.23%)	0 / 14 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

Non-serious adverse events	Cohort 2	Cohort 1	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	30 / 31 (96.77%)	12 / 14 (85.71%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Anogenital warts			
subjects affected / exposed	0 / 31 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Seborrhoeic keratosis			
subjects affected / exposed	1 / 31 (3.23%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			
Superior vena cava syndrome			
subjects affected / exposed	1 / 31 (3.23%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Vena cava thrombosis			
subjects affected / exposed	0 / 31 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Hypotension			
subjects affected / exposed	1 / 31 (3.23%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Hypertension			
subjects affected / exposed	2 / 31 (6.45%)	0 / 14 (0.00%)	
occurrences (all)	3	0	
Haematoma			
subjects affected / exposed	1 / 31 (3.23%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Deep vein thrombosis			
subjects affected / exposed	1 / 31 (3.23%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Raynaud's phenomenon			
subjects affected / exposed	1 / 31 (3.23%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Asthenia			

subjects affected / exposed	9 / 31 (29.03%)	1 / 14 (7.14%)	
occurrences (all)	16	2	
Chest pain			
subjects affected / exposed	3 / 31 (9.68%)	0 / 14 (0.00%)	
occurrences (all)	3	0	
Fatigue			
subjects affected / exposed	4 / 31 (12.90%)	2 / 14 (14.29%)	
occurrences (all)	6	2	
Chills			
subjects affected / exposed	1 / 31 (3.23%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
General physical health deterioration			
subjects affected / exposed	1 / 31 (3.23%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Injection site haematoma			
subjects affected / exposed	0 / 31 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Non-cardiac chest pain			
subjects affected / exposed	0 / 31 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Oedema peripheral			
subjects affected / exposed	3 / 31 (9.68%)	0 / 14 (0.00%)	
occurrences (all)	4	0	
Pyrexia			
subjects affected / exposed	1 / 31 (3.23%)	1 / 14 (7.14%)	
occurrences (all)	1	1	
Systemic inflammatory response syndrome			
subjects affected / exposed	1 / 31 (3.23%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Influenza like illness			
subjects affected / exposed	0 / 31 (0.00%)	3 / 14 (21.43%)	
occurrences (all)	0	4	
Immune system disorders			
Cytokine release syndrome			

subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	1 / 14 (7.14%) 1	
Reproductive system and breast disorders Gynaecomastia subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 14 (0.00%) 0	
Respiratory, thoracic and mediastinal disorders Rhinorrhoea subjects affected / exposed occurrences (all)	3 / 31 (9.68%) 3	0 / 14 (0.00%) 0	
Productive cough subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 14 (0.00%) 0	
Pneumonitis subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	1 / 14 (7.14%) 1	
Lung disorder subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	1 / 14 (7.14%) 1	
Dyspnoea exertional subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 2	0 / 14 (0.00%) 0	
Dyspnoea subjects affected / exposed occurrences (all)	3 / 31 (9.68%) 4	3 / 14 (21.43%) 3	
Cough subjects affected / exposed occurrences (all)	5 / 31 (16.13%) 7	3 / 14 (21.43%) 3	
Psychiatric disorders Bulimia nervosa subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	1 / 14 (7.14%) 1	
Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	1 / 14 (7.14%) 1	

Aspartate aminotransferase increased			
subjects affected / exposed	0 / 31 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 31 (3.23%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 31 (3.23%)	1 / 14 (7.14%)	
occurrences (all)	1	1	
Blood creatinine increased			
subjects affected / exposed	0 / 31 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Blood potassium increased			
subjects affected / exposed	1 / 31 (3.23%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
C-reactive protein increased			
subjects affected / exposed	1 / 31 (3.23%)	1 / 14 (7.14%)	
occurrences (all)	1	1	
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 31 (3.23%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Weight increased			
subjects affected / exposed	2 / 31 (6.45%)	1 / 14 (7.14%)	
occurrences (all)	2	1	
Weight decreased			
subjects affected / exposed	1 / 31 (3.23%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Lipase increased			
subjects affected / exposed	0 / 31 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	14	
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 31 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	

Compression fracture subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 14 (0.00%) 0	
Fall subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 14 (0.00%) 0	
Infusion related reaction subjects affected / exposed occurrences (all)	2 / 31 (6.45%) 6	0 / 14 (0.00%) 0	
Ligament sprain subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 14 (0.00%) 0	
Cardiac disorders Tachycardia subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 14 (0.00%) 0	
Sinus tachycardia subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 14 (0.00%) 0	
Nervous system disorders Neuralgia subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 14 (0.00%) 0	
Ataxia subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 14 (0.00%) 0	
Balance disorder subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 14 (0.00%) 0	
Carpal tunnel syndrome subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 14 (0.00%) 0	
Dizziness subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	1 / 14 (7.14%) 1	
Headache			

subjects affected / exposed	2 / 31 (6.45%)	2 / 14 (14.29%)	
occurrences (all)	3	2	
Syncope			
subjects affected / exposed	1 / 31 (3.23%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Sciatica			
subjects affected / exposed	0 / 31 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Polyneuropathy			
subjects affected / exposed	1 / 31 (3.23%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Peripheral sensory neuropathy			
subjects affected / exposed	4 / 31 (12.90%)	1 / 14 (7.14%)	
occurrences (all)	4	1	
Paraesthesia			
subjects affected / exposed	1 / 31 (3.23%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Neuropathy peripheral			
subjects affected / exposed	1 / 31 (3.23%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Taste disorder			
subjects affected / exposed	1 / 31 (3.23%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 31 (12.90%)	1 / 14 (7.14%)	
occurrences (all)	4	5	
Neutropenia			
subjects affected / exposed	1 / 31 (3.23%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Eosinophilia			
subjects affected / exposed	0 / 31 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Autoimmune haemolytic anaemia			
subjects affected / exposed	1 / 31 (3.23%)	0 / 14 (0.00%)	
occurrences (all)	1	0	

Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	2 / 31 (6.45%) 2	1 / 14 (7.14%) 1	
Eye disorders Chalazion subjects affected / exposed occurrences (all) Periorbital swelling subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1 0 / 31 (0.00%) 0	0 / 14 (0.00%) 0 1 / 14 (7.14%) 1	
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) Abdominal pain upper subjects affected / exposed occurrences (all) Angular cheilitis subjects affected / exposed occurrences (all) Aphthous ulcer subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Odynophagia subjects affected / exposed occurrences (all) Stomatitis	2 / 31 (6.45%) 2 4 / 31 (12.90%) 4 1 / 31 (3.23%) 1 1 / 31 (3.23%) 1 2 / 31 (6.45%) 2 2 / 31 (6.45%) 3 5 / 31 (16.13%) 6 1 / 31 (3.23%) 3	1 / 14 (7.14%) 1 0 / 14 (0.00%) 0 0 / 14 (0.00%) 0 0 / 14 (0.00%) 0 2 / 14 (14.29%) 2 1 / 14 (7.14%) 1 0 / 14 (0.00%) 0	

subjects affected / exposed occurrences (all)	3 / 31 (9.68%) 4	0 / 14 (0.00%) 0	
Vomiting subjects affected / exposed occurrences (all)	3 / 31 (9.68%) 3	2 / 14 (14.29%) 2	
Hepatobiliary disorders Hepatitis subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 14 (0.00%) 0	
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all)	3 / 31 (9.68%) 3	1 / 14 (7.14%) 1	
Erythema subjects affected / exposed occurrences (all)	2 / 31 (6.45%) 3	0 / 14 (0.00%) 0	
Dry skin subjects affected / exposed occurrences (all)	2 / 31 (6.45%) 2	3 / 14 (21.43%) 3	
Dermatitis acneiform subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 14 (0.00%) 0	
Acne subjects affected / exposed occurrences (all)	2 / 31 (6.45%) 2	0 / 14 (0.00%) 0	
Urticaria subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	2 / 14 (14.29%) 2	
Rash maculo-papular subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	2 / 14 (14.29%) 3	
Rash subjects affected / exposed occurrences (all)	2 / 31 (6.45%) 3	2 / 14 (14.29%) 2	
Purpura			

subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 14 (0.00%) 0	
Vitiligo subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	1 / 14 (7.14%) 1	
Renal and urinary disorders			
Calculus urethral subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 14 (0.00%) 0	
Pollakiuria subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	1 / 14 (7.14%) 1	
Renal colic subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 14 (0.00%) 0	
Urinary tract pain subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 14 (0.00%) 0	
Endocrine disorders			
Autoimmune thyroiditis subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 14 (0.00%) 0	
Hyperadrenocorticism subjects affected / exposed occurrences (all)	0 / 31 (0.00%) 0	1 / 14 (7.14%) 1	
Hyperthyroidism subjects affected / exposed occurrences (all)	2 / 31 (6.45%) 2	0 / 14 (0.00%) 0	
Hypothyroidism subjects affected / exposed occurrences (all)	4 / 31 (12.90%) 4	1 / 14 (7.14%) 1	
Adrenocorticotrophic hormone deficiency subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1	0 / 14 (0.00%) 0	
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	2 / 31 (6.45%)	1 / 14 (7.14%)	
occurrences (all)	2	2	
Back pain			
subjects affected / exposed	2 / 31 (6.45%)	1 / 14 (7.14%)	
occurrences (all)	2	1	
Muscle spasms			
subjects affected / exposed	3 / 31 (9.68%)	1 / 14 (7.14%)	
occurrences (all)	4	1	
Myalgia			
subjects affected / exposed	0 / 31 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Neck pain			
subjects affected / exposed	0 / 31 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	2	
Pain in extremity			
subjects affected / exposed	1 / 31 (3.23%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Onychomycosis			
subjects affected / exposed	0 / 31 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Balanoposthitis infective			
subjects affected / exposed	0 / 31 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Bronchitis			
subjects affected / exposed	3 / 31 (9.68%)	2 / 14 (14.29%)	
occurrences (all)	3	3	
COVID-19			
subjects affected / exposed	3 / 31 (9.68%)	1 / 14 (7.14%)	
occurrences (all)	3	1	
Conjunctivitis			
subjects affected / exposed	0 / 31 (0.00%)	2 / 14 (14.29%)	
occurrences (all)	0	2	
Cystitis			

subjects affected / exposed	1 / 31 (3.23%)	0 / 14 (0.00%)
occurrences (all)	1	0
Dermo-hypodermatitis		
subjects affected / exposed	1 / 31 (3.23%)	0 / 14 (0.00%)
occurrences (all)	1	0
Folliculitis		
subjects affected / exposed	1 / 31 (3.23%)	1 / 14 (7.14%)
occurrences (all)	1	1
Fungal skin infection		
subjects affected / exposed	0 / 31 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	1
Gastroenteritis		
subjects affected / exposed	0 / 31 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	1
Influenza		
subjects affected / exposed	0 / 31 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	1
Localised infection		
subjects affected / exposed	0 / 31 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	1
Oesophageal candidiasis		
subjects affected / exposed	1 / 31 (3.23%)	0 / 14 (0.00%)
occurrences (all)	1	0
Nasopharyngitis		
subjects affected / exposed	2 / 31 (6.45%)	1 / 14 (7.14%)
occurrences (all)	2	1
Oral infection		
subjects affected / exposed	0 / 31 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	1
Otitis externa		
subjects affected / exposed	0 / 31 (0.00%)	1 / 14 (7.14%)
occurrences (all)	0	1
Pharyngitis		
subjects affected / exposed	1 / 31 (3.23%)	1 / 14 (7.14%)
occurrences (all)	1	1
Rash pustular		

subjects affected / exposed	1 / 31 (3.23%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Respiratory tract infection			
subjects affected / exposed	0 / 31 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Rhinitis			
subjects affected / exposed	3 / 31 (9.68%)	1 / 14 (7.14%)	
occurrences (all)	3	1	
Sinusitis			
subjects affected / exposed	2 / 31 (6.45%)	0 / 14 (0.00%)	
occurrences (all)	3	0	
Skin infection			
subjects affected / exposed	0 / 31 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Tracheitis			
subjects affected / exposed	1 / 31 (3.23%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Upper respiratory tract infection			
subjects affected / exposed	2 / 31 (6.45%)	1 / 14 (7.14%)	
occurrences (all)	2	1	
Urinary tract infection			
subjects affected / exposed	1 / 31 (3.23%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 31 (0.00%)	1 / 14 (7.14%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Folate deficiency			
subjects affected / exposed	1 / 31 (3.23%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Decreased appetite			
subjects affected / exposed	4 / 31 (12.90%)	1 / 14 (7.14%)	
occurrences (all)	4	1	
Hypercalcaemia			
subjects affected / exposed	1 / 31 (3.23%)	0 / 14 (0.00%)	
occurrences (all)	2	0	

Hyperkalaemia			
subjects affected / exposed	1 / 31 (3.23%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Hypokalaemia			
subjects affected / exposed	1 / 31 (3.23%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Steroid diabetes			
subjects affected / exposed	1 / 31 (3.23%)	0 / 14 (0.00%)	
occurrences (all)	1	0	
Dyslipidaemia			
subjects affected / exposed	1 / 31 (3.23%)	0 / 14 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 October 2019	Amendment 1.0 23 October 2019
26 November 2019	Amendment 2.0 26 November 2019
03 December 2020	Amendment 3.0 03 December 2020
05 August 2021	Amendment 4.0 05 August 2021

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported