Clinical trial results:
A phase II study of brentuximab vedotin in patients with relapsed or refractory peripheral T-cell lymphoma treated with gemcitabine followed by brentuximab vedotin maintenance

Summary

EudraCT number	2017-000409-19
Trial protocol	BE
Global end of trial date	08 October 2022

Results information

Result version number	v1 (current)
This version publication date	04 May 2025
First version publication date	04 May 2025

Trial information

Trial identification

Sponsor protocol code	TOTAL

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	LYSARC
Sponsor organisation address	Centre hospitalier Lyon Sud, PIERRE BENITE, France,
Public contact	Management de Projet M. Bonhomme, LYSARC, +33 472 66 93 33, affaires-reglementaires@lysarc.org
Scientific contact	Management de Projet M. Bonhomme, LYSARC, +33 472 66 93 33, affaires-reglementaires@lysarc.org

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	09 October 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	08 October 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the efficacy of brentuximab vedotin (BV) in patients treated by gemcitabine for relapsed or refractory peripheral T-cell lymphoma in term of overall response rate assessed after 4 cycles of treatment according to the international response criteria for malignant lymphoma (Lugano Classification 2014 – CT-Based Response).

Protection of trial subjects:

no specific measures

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 January 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 11
Country: Number of subjects enrolled	France: 60
Worldwide total number of subjects	71
EEA total number of subjects	71

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)	31
From 65 to 84 years	40
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The recruitment was performed from 10-April-2018 to 08-October-2019.

Pre-assignment

Screening details:

The subject’s eligibility is evaluated during the baseline period prior to the first administration of the study drug.

Period 1

Period 1 title	induction period
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	experimental

Arm description: -

Arm type	Experimental
Investigational medicinal product name	brentuximab vedotin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for dispersion for infusion
Routes of administration	Infusion

Dosage and administration details:

Brentuximab vedotin: 1.8 mg/kg at D8 of a 28-day cycle
reconstitution : Brentuximab vedotin must be reconstituted with 10.5 mL of Sterile Water for Injection, gently swirling the vial until the contents are completely dissolved.
Dilution: The appropriate amount of reconstituted brentuximab vedotin will be withdrawn from the vial(s) and diluted in a 150 mL infusion bag containing 0.9% Sodium Chloride Injection.

Number of subjects in period 1	experimental
Started	71
Completed	45
Not completed	26
Adverse event, serious fatal	3
progression	21
Adverse event, non-fatal	2

Period 2

Period 2 title	maintenance period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	experimental

Arm description: -

Arm type	Experimental
Investigational medicinal product name	brentuximab vedotin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for dispersion for infusion
Routes of administration	Infusion

Dosage and administration details:

Brentuximab vedotin: 1.8 mg/kg at D1 of a 21-day cycle
reconstitution : Brentuximab vedotin must be reconstituted with 10.5 mL of Sterile Water for Injection, gently swirling the vial until the contents are completely dissolved.
Dilution: The appropriate amount of reconstituted brentuximab vedotin will be withdrawn from the vial(s) and diluted in a 150 mL infusion bag containing 0.9% Sodium Chloride Injection.

Number of subjects in period 2[1]	experimental
Started	28
Completed	8
Not completed	20
transplantation	5
progression	4
Adverse event, non-fatal	10
Protocol deviation	1

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: 17 patients permanently discontinued the treatment after the end of induction period.
Reasons for treatment discontinuation:
- 11 for progression
- 4 for other reasons
- 1 for protocol deviation
- 1 for withdrawal by subject

Period 3

Period 3 title	follow up
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	experimental
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	brentuximab vedotin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for dispersion for infusion
Routes of administration	Infusion

Dosage and administration details:
no administration during follow up period

Number of subjects in period 3	experimental
Started	8
Completed	8

Baseline characteristics

Reporting groups

Reporting group title	induction period

Reporting group description: -

Reporting group values	induction period	Total	
Number of subjects	71	71	
Age categorical Units: Subjects			
From 18-60 years	23	23	
61 years and over	48	48	
Age continuous Units: years			
median	66		
full range (min-max)	20 to 79	-	
Gender categorical Units: Subjects			
Female	24	24	
Male	47	47	
Ann Arbor stage Units: Subjects			
I-II	6	6	
III-IV	65	65	
ECOG Units: Subjects			
0-1	55	55	
2-3-4	16	16	
IPI Units: Subjects			
Low risk	8	8	
Intermediate-low risk	18	18	
Intermediate-high risk	25	25	
High risk	20	20	

Subject analysis sets

Subject analysis set title	FAS
Subject analysis set type	Full analysis

Subject analysis set description:

The Full Analysis set (FAS) includes all patients having signed the informed consent and who received at least one dose of the induction therapy (any drug).

Reporting group values	FAS		
Number of subjects	71		
Age categorical Units: Subjects			
From 18-60 years	23		
61 years and over	48		

Age continuous Units: years			
median	66		
full range (min-max)	20 to 79		
Gender categorical Units: Subjects			
Female	24		
Male	47		
Ann Arbor stage Units: Subjects			
I-II	6		
III-IV	65		
ECOG Units: Subjects			
0-1	55		
2-3-4	16		
IPI Units: Subjects			
Low risk	8		
Intermediate-low risk	18		
Intermediate-high risk	25		
High risk	20		

End points

End points reporting groups

Reporting group title	experimental
Reporting group description: -	
Reporting group title	experimental
Reporting group description: -	
Reporting group title	experimental
Reporting group description: -	
Subject analysis set title	FAS
Subject analysis set type	Full analysis

Subject analysis set description:

The Full Analysis set (FAS) includes all patients having signed the informed consent and who received at least one dose of the induction therapy (any drug).

Primary: ORR at the end of induction

End point title	ORR at the end of induction[1]

End point description:

Assessment of response are based on the Lugano Classification 2014 (CT-Based Response).
Patient without response assessment (due to whatever reason) are considered as non-responder.
ORR = CR + PR

End point type	Primary

End point timeframe:

End of induction (4 cycles)

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: As there is only one treatment arm, no comparison was planned for the primary criterion.

End point values	FAS			
Subject group type	Subject analysis set			
Number of subjects analysed	71			
Units: percentage				
number (confidence interval 90%)	46.5 (36.30 to 56.89)			

Statistical analyses

No statistical analyses for this end point

Secondary: CRR at the end of induction

End point title	CRR at the end of induction

End point description:

Assessment of response are based on the Lugano Classification 2014 (CT-Based Response).
Patient without response assessment (due to whatever reason) are considered as non-responder.
CRR = CR

End point type	Secondary

End point timeframe:

End of induction (4 cycles)

End point values	FAS			
Subject group type	Subject analysis set			
Number of subjects analysed	71			
Units: percent				
number (confidence interval 90%)	19.7 (12.33 to 29.10)			

Statistical analyses

No statistical analyses for this end point

Secondary: OMR at the end of induction

End point title	OMR at the end of induction

End point description:

Assessment of response are based on the Lugano Classification 2014 (CT-Based Response).
Patient without response assessment (due to whatever reason) are considered as non-responder.
ORR = CR + PR

End point type	Secondary

End point timeframe:

End of induction (4 cycles)

End point values	FAS			
Subject group type	Subject analysis set			
Number of subjects analysed	71			
Units: percent				
number (confidence interval 90%)	45.1 (34.96 to 55.50)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free survival

End point title	Progression-free survival

End point description:

If a subject has not progressed or died, PFS will be censored at the time of last visit with adequate assessment.

End point type	Secondary

End point timeframe:

PFS is defined as the time from inclusion into the study to the first observation of documented disease progression/relapse or death due to any cause.

End point values	FAS			
Subject group type	Subject analysis set			
Number of subjects analysed	71			
Units: month				
median (confidence interval 95%)	4.5 (3.5 to 10)			

Attachments (see zip file)	pfs total.jpg

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival

End point title	Overall survival

End point description:

Alive patients will be censored at their last contact.

End point type	Secondary

End point timeframe:

Overall survival will be measured from the date of inclusion to the date of death from any cause.

End point values	FAS			
Subject group type	Subject analysis set			
Number of subjects analysed	71			
Units: month				
median (confidence interval 95%)	12.9 (9 to 29.6)			

Attachments (see zip file)	os total.jpg

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of response

End point title	Duration of response

End point description:

Patients alive and free of progression will be censored at their last visit with adequate assessment.

End point type	Secondary

End point timeframe:

Duration of response will be measured from the time of attainment of CR or PR to the date of first documented disease progression, relapse or death from any cause.

End point values	FAS			
Subject group type	Subject analysis set			
Number of subjects analysed	71			
Units: month				
median (full range (min-max))	15.8 (4.9 to 45)			

Attachments (see zip file)	dor total.jpg

Statistical analyses

No statistical analyses for this end point

Secondary: Time to next treatment

End point title	Time to next treatment

End point description:

Patients without documented event at the time of analysis will be censored on their last tumor assessment.

End point type	Secondary

End point timeframe:

Time to next treatment is defined as the time from the date of inclusion to the death (due to any cause) or first documented administration of any new anti-lymphoma treatment (different to study treatment and treatment for progression).

End point values	FAS			
Subject group type	Subject analysis set			
Number of subjects analysed	71			
Units: month				
median (confidence interval 95%)	9.4 (6 to 13.4)			

Attachments (see zip file)	ttnt total.jpg

Statistical analyses

No statistical analyses for this end point

Secondary: Time to treatment failure

End point title	Time to treatment failure

End point description:

Patients who completed treatment will be censored at the end of GBv treatment evaluation.

End point type	Secondary

End point timeframe:

TTF is defined as the time from the date of inclusion to the date of first documented treatment discontinuation for any reason, including disease progression, treatment toxicity, and deaths.

End point values	FAS			
Subject group type	Subject analysis set			
Number of subjects analysed	71			
Units: month				
median (confidence interval 95%)	3.9 (3.2 to 4.2)			

Attachments (see zip file)	ttf total.jpg

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events will be reported from signature of informed consent up to end of treatment visit (16 weeks for patients not included in the maintenance period, up to 56 weeks after the last study drug administration of the maintenance period).

Assessment type	Non-systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	4.03

Reporting groups

Reporting group title	induction phase
Reporting group description: -	
Reporting group title	maintenance phase

Reporting group description: -

Serious adverse events	induction phase	maintenance phase	
Total subjects affected by serious adverse events			
subjects affected / exposed	18 / 71 (25.35%)	5 / 28 (17.86%)	
number of deaths (all causes)	42	0	
number of deaths resulting from adverse events	5	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
BASAL CELL CARCINOMA			
subjects affected / exposed	1 / 71 (1.41%)	1 / 28 (3.57%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
SQUAMOUS CELL CARCINOMA			
subjects affected / exposed	0 / 71 (0.00%)	1 / 28 (3.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	2 / 71 (2.82%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			

subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
DIZZINESS			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
NEUROPATHY PERIPHERAL			
subjects affected / exposed	0 / 71 (0.00%)	1 / 28 (3.57%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
POLYNEUROPATHY			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
General physical health deterioration			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	0 / 71 (0.00%)	1 / 28 (3.57%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden death			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	

GENERALISED OEDEMA			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
FEBRILE NEUTROPENIA			
subjects affected / exposed	2 / 71 (2.82%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ANAEMIA			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
ABDOMINAL PAIN			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COLITIS			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
DIARRHOEA			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
LIVER DISORDER			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (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			
RESPIRATORY DISTRESS			

subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Skin and subcutaneous tissue disorders			
TOXIC SKIN ERUPTION			
subjects affected / exposed	2 / 71 (2.82%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
RASH MACULO-PAPULAR			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (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			
ARTHRALGIA			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ARTHRITIS			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	2 / 71 (2.82%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Sepsis			
subjects affected / exposed	2 / 71 (2.82%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	1 / 2	0 / 0	
Cytomegalovirus chorioretinitis			
subjects affected / exposed	0 / 71 (0.00%)	1 / 28 (3.57%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Escherichia urinary tract infection			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Skin infection			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	induction phase	maintenance phase	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	64 / 71 (90.14%)	20 / 28 (71.43%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
BASAL CELL CARCINOMA			

subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
SQUAMOUS CELL CARCINOMA			
subjects affected / exposed	0 / 71 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
Vascular disorders			
HYPERTENSION			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
PERIPHERAL ARTERIAL OCCLUSIVE DISEASE			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
THROMBOPHLEBITIS SUPERFICIAL			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
VENOUS THROMBOSIS LIMB			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
ASTHENIA			
subjects affected / exposed	6 / 71 (8.45%)	0 / 28 (0.00%)	
occurrences (all)	7	0	
FATIGUE			
subjects affected / exposed	2 / 71 (2.82%)	0 / 28 (0.00%)	
occurrences (all)	2	0	
GENERAL PHYSICAL HEALTH DETERIORATION			
subjects affected / exposed	2 / 71 (2.82%)	0 / 28 (0.00%)	
occurrences (all)	2	0	
GENERALISED OEDEMA			
subjects affected / exposed	2 / 71 (2.82%)	0 / 28 (0.00%)	
occurrences (all)	2	0	
PYREXIA			
subjects affected / exposed	2 / 71 (2.82%)	0 / 28 (0.00%)	
occurrences (all)	2	0	
MALAISE			

subjects affected / exposed	0 / 71 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
OEDEMA PERIPHERAL			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
SUDDEN DEATH			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
FEMALE GENITAL TRACT FISTULA			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
LUNG DISORDER			
subjects affected / exposed	3 / 71 (4.23%)	0 / 28 (0.00%)	
occurrences (all)	3	0	
DYSPNOEA			
subjects affected / exposed	1 / 71 (1.41%)	1 / 28 (3.57%)	
occurrences (all)	1	1	
RESPIRATORY DISTRESS			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
CONFUSIONAL STATE			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
IRRITABILITY			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Investigations			
WEIGHT INCREASED			
subjects affected / exposed	1 / 71 (1.41%)	1 / 28 (3.57%)	
occurrences (all)	1	1	
ALANINE AMINOTRANSFERASE INCREASED			

subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
GAMMA-GLUTAMYLTRANSFERASE INCREASED			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
LIPASE INCREASED			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
WEIGHT DECREASED			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
CARDIAC FAILURE			
subjects affected / exposed	2 / 71 (2.82%)	0 / 28 (0.00%)	
occurrences (all)	2	0	
MITRAL VALVE DISEASE			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
MYOCARDIAL INFARCTION			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
VENTRICULAR EXTRASYSTOLES			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
NEUROPATHY PERIPHERAL			
subjects affected / exposed	3 / 71 (4.23%)	10 / 28 (35.71%)	
occurrences (all)	3	10	
PERIPHERAL SENSORY NEUROPATHY			
subjects affected / exposed	3 / 71 (4.23%)	4 / 28 (14.29%)	
occurrences (all)	3	4	
POLYNEUROPATHY			
subjects affected / exposed	3 / 71 (4.23%)	0 / 28 (0.00%)	
occurrences (all)	3	0	
DIZZINESS			

subjects affected / exposed	2 / 71 (2.82%)	0 / 28 (0.00%)	
occurrences (all)	2	0	
PERIPHERAL MOTOR NEUROPATHY			
subjects affected / exposed	0 / 71 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
neutropenia			
subjects affected / exposed	39 / 71 (54.93%)	6 / 28 (21.43%)	
occurrences (all)	75	6	
anaemia			
subjects affected / exposed	20 / 71 (28.17%)	0 / 28 (0.00%)	
occurrences (all)	30	0	
leukopenia			
subjects affected / exposed	12 / 71 (16.90%)	0 / 28 (0.00%)	
occurrences (all)	23	0	
thrombocytopenia			
subjects affected / exposed	10 / 71 (14.08%)	0 / 28 (0.00%)	
occurrences (all)	15	0	
lymphopenia			
subjects affected / exposed	3 / 71 (4.23%)	0 / 28 (0.00%)	
occurrences (all)	4	0	
febrile netropenia			
subjects affected / exposed	2 / 71 (2.82%)	0 / 28 (0.00%)	
occurrences (all)	2	0	
Eye disorders			
CATARACT			
subjects affected / exposed	0 / 71 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
DIARRHOEA			
subjects affected / exposed	3 / 71 (4.23%)	0 / 28 (0.00%)	
occurrences (all)	4	0	
NAUSEA			
subjects affected / exposed	3 / 71 (4.23%)	0 / 28 (0.00%)	
occurrences (all)	4	0	
ABDOMINAL PAIN			

subjects affected / exposed	2 / 71 (2.82%)	0 / 28 (0.00%)	
occurrences (all)	2	0	
COLITIS			
subjects affected / exposed	2 / 71 (2.82%)	0 / 28 (0.00%)	
occurrences (all)	2	0	
CONSTIPATION			
subjects affected / exposed	2 / 71 (2.82%)	0 / 28 (0.00%)	
occurrences (all)	2	0	
ANAL HAEMORRHAGE			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences (all)	2	0	
VOMITING			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Hepatobiliary disorders			
HEPATIC CYTOLYSIS			
subjects affected / exposed	2 / 71 (2.82%)	0 / 28 (0.00%)	
occurrences (all)	2	0	
LIVER DISORDER			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
PRURITUS			
subjects affected / exposed	2 / 71 (2.82%)	1 / 28 (3.57%)	
occurrences (all)	2	1	
RASH			
subjects affected / exposed	2 / 71 (2.82%)	0 / 28 (0.00%)	
occurrences (all)	3	0	
TOXIC SKIN ERUPTION			
subjects affected / exposed	2 / 71 (2.82%)	0 / 28 (0.00%)	
occurrences (all)	2	0	
RASH MACULO-PAPULAR			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
SKIN DISORDER			

subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
URTICARIA			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
ARTHRITIS			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
ARTHROPATHY			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
MUSCLE SPASMS			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences (all)	2	0	
OSTEOARTHRITIS			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
ROTATOR CUFF SYNDROME			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
SYNOVITIS			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
bronchitis			
subjects affected / exposed	2 / 71 (2.82%)	3 / 28 (10.71%)	
occurrences (all)	2	3	
pneumonia			
subjects affected / exposed	4 / 71 (5.63%)	0 / 28 (0.00%)	
occurrences (all)	4	0	
clostridium difficile infection			

subjects affected / exposed	2 / 71 (2.82%)	0 / 28 (0.00%)	
occurrences (all)	2	0	
sepsis			
subjects affected / exposed	2 / 71 (2.82%)	0 / 28 (0.00%)	
occurrences (all)	2	0	
campylobacter infection			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
clostridium difficile colitis			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
conjunctivitis			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
cytomegalovirus chorioretinitis			
subjects affected / exposed	0 / 71 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
device related infection			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
escherichia urinary tract infection			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
folliculitis			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
hordeolum			
subjects affected / exposed	0 / 71 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
infection			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
nasopharyngitis			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
paronychia			

subjects affected / exposed	0 / 71 (0.00%)	1 / 28 (3.57%)		
occurrences (all)	0	1		
PNEUMOCYSTIS JIROVECII PNEUMONIA				
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)		
occurrences (all)	1	0		
PNEUMONIA BACTERIAL				
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)		
occurrences (all)	1	0		
PSEUDOMONAS INFECTION				
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)		
occurrences (all)	1	0		
SEPTIC SHOCK				
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)		
occurrences (all)	2	0		
SKIN INFECTION				
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)		
occurrences (all)	1	0		
TONSILLITIS				
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)		
occurrences (all)	1	0		
TOOTH ABSCESS				
subjects affected / exposed	0 / 71 (0.00%)	1 / 28 (3.57%)		
occurrences (all)	0	1		
TOOTH INFECTION				
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)		
occurrences (all)	1	0		
TRACHEITIS				
subjects affected / exposed	0 / 71 (0.00%)	1 / 28 (3.57%)		
occurrences (all)	0	1		
UPPER RESPIRATORY TRACT INFECTION				
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)		
occurrences (all)	1	0		
URINARY TRACT INFECTION				

subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
VIRAL UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
DECREASED APPETITE			
subjects affected / exposed	2 / 71 (2.82%)	0 / 28 (0.00%)	
occurrences (all)	2	0	
HYPOKALAEMIA			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
HYPONATRAEMIA			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences (all)	1	0	
IRON DEFICIENCY			
subjects affected / exposed	0 / 71 (0.00%)	1 / 28 (3.57%)	
occurrences (all)	0	1	
TUMOUR LYSIS SYNDROME			
subjects affected / exposed	1 / 71 (1.41%)	0 / 28 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 November 2018	change of coordinating investigator + change in the number of IDMCs

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported