Clinical trial results:
A Prospective Multicenter Phase 2 Study of the Chemotherapy-Free Combination of the Intravenous Phosphatidylinositol-3-Kinase (PI3K) Inhibitor Copanlisib in Combination with Obinutuzumab in Patients with Previously Untreated Follicular Lymphoma (FL) and a High Tumor Burden.

Summary

EudraCT number	2018-004038-13
Trial protocol	DE
Global end of trial date	28 January 2025

Results information

Result version number	v1 (current)
This version publication date	11 June 2026
First version publication date	11 June 2026

Trial information

Trial identification

Sponsor protocol code	ALTERNATIVE-C

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Klinikum der Universität München
Sponsor organisation address	Marchioninistr. 15, München, Germany, 81377
Public contact	Dr. Christian Schmidt, LMU Klinikum, Medizinische Klinik III, Studienzentrale für Hämatologie , 0049 89440077907, Christian_Schmidt@med.uni-muenchen.de
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Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	06 October 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 January 2025
Global end of trial reached?	Yes
Global end of trial date	28 January 2025
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to evaluate the efficacy of the chemotherapy-free combination of copanlisib and obinutuzumab in patients with previously untreated follicular lymphoma (FL) and a high tumor burden. Primary endpoint is the probability of progression free survival one year after registration. Progression-free survival (PFS) is chosen as primary endpoint since it represents besides overall survival the most relevant parameter for patients.
PFS is defined as the time from registration to lymphoma progression or death from any cause.

Protection of trial subjects:

The protocol, protocol amendments, informed consent form, Investigator’s Brochure, and other relevant documents were reviewed and approved by an independent ethics committee before the study was initiated. Written informed consent was obtained from all participants prior to study entry. Participants were free to withdraw from the study at any time without providing a reason, and any interventional procedure could be declined by the participants.

Background therapy:

No background therapy

Evidence for comparator: -

Actual start date of recruitment	15 May 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	Germany: 102
Worldwide total number of subjects	102
EEA total number of subjects	102

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)	65
From 65 to 84 years	36
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

First patient in: 29 October 2020, last patient in: 16 September 2022

Pre-assignment

Screening details:

Subjects had to fulfill all the inclusion criteria defined in the study protocol. Subjects who met any of the exclusion criteria were not eligible for participation in the study.
Of 105 subjects screened, 3 were screening failures: 1 DLBCL, 1 concomitant malignancy, and 1 withdrew consent before registration.

Period 1

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

Arms

Arm title	Copanlisib + Obinutuzumab

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Copanlisib
Investigational medicinal product code	BAY 80-6946
Other name	ALIQOPA
Pharmaceutical forms	Powder for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Induction: intravenous infusion at a dose of 60 mg on day 1, 8, 15 of cycles 1-6.
Consolidation: intravenous infusion at a dose of 60 mg on days 1 and 15 of cycles 7-12.
Maintenance: intravenous infusion at a dose of 60 mg every 8 weeks.

Investigational medicinal product name	Obinutuzumab
Investigational medicinal product code	
Other name	GAZYVARO
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Induction: intravenous infusion at a dose of 1000 mg on days 1, 8, 15 of cycle 1 and on day 1 of cycles 2-6.
Consolidation: intravenous infusion at a dose of 1000 mg every 8 weeks.
Maintenance: intravenous infusion at a dose of 1000 mg every 8 weeks.

Number of subjects in period 1	Copanlisib + Obinutuzumab
Started	102
Completed	96
Not completed	6
Consent withdrawn by subject	1
Adverse event, non-fatal	2

Change of diagnosis to DLBCL	1
Protocol deviation	2

Baseline characteristics

Reporting groups	
Reporting group title	Overall period

Reporting group description: -

Reporting group values	Overall period	Total	
Number of subjects	102	102	
Age categorical Units: Subjects			
>60 years	50	50	
<=60 years	52	52	
Age continuous Units: years			
median	60		
full range (min-max)	30 to 85	-	
Gender categorical Units: Subjects			
Female	47	47	
Male	55	55	
Histology Units: Subjects			
FL grade 1	18	18	
FL grade 2	68	68	
FL grade 3a	15	15	
DLBCL	1	1	
Ann Arbor stage Units: Subjects			
II	16	16	
III	40	40	
IV	46	46	
LDH			
LDH > upper normal			
Units: Subjects			
> upper normal	30	30	
<= upper normal	70	70	
Not recorded	2	2	
Hemoglobin Units: Subjects			
<12g/dL	18	18	
>=12g/dL	82	82	
Not recorded	2	2	
Involved nodal areas Units: Subjects			
>4	40	40	
<=4	62	62	
FLIPI risk factors Units: Subjects			

n=0	5	5	
n=1	23	23	
n=2	32	32	
n=3	31	31	
n=4	8	8	
n=5	3	3	
ECOG performance status Units: Subjects			
ECOG=0	72	72	
ECOG=1	28	28	
ECOG=2	2	2	
B-symptoms Units: Subjects			
Present	33	33	
Absent	68	68	
Not recorded	1	1	
Fever Units: Subjects			
Present	3	3	
Absent	98	98	
Not recorded	1	1	
Loss of weight Units: Subjects			
Present	14	14	
Absent	87	87	
Not recorded	1	1	
Night sweats Units: Subjects			
Present	24	24	
Absent	77	77	
Not recorded	1	1	

End points

End points reporting groups

Reporting group title	Copanlisib + Obinutuzumab
Reporting group description: -	
Subject analysis set title	Copanlisib + Obinutuzumab
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All registered patients	

Primary: 1-year progression free survival

End point title	1-year progression free survival
End point description:	
The primary outcome is the rate of patients achieving a progression-free survival (PFS) of more than one year from study registration. PFS is defined as time from registration to lymphoma progression or death from any cause.	
End point type	Primary
End point timeframe:	
From registration to one year after registration	

End point values	Copanlisib + Obinutuzumab	Copanlisib + Obinutuzumab		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	93	93		
Units: subjects				
PFS event within 1 year from registration	15	15		
No PFS event within 1 year from registration	78	78		

Statistical analyses

Statistical analysis title	Evaluation of primary outcome
Statistical analysis description:	
A one-sided binomiat test was used to test if the the rate of 1-year PFS was significantly higher than the pre-specified value of 85%. There was no comparison between groups, the test was done in 93 evaluable patients.	
Comparison groups	Copanlisib + Obinutuzumab v Copanlisib + Obinutuzumab
Number of subjects included in analysis	186
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.68
Method	one-sided binomial test
Parameter estimate	rate
Point estimate	0.84

Confidence interval	
level	95 %
sides	1-sided
lower limit	0.76

Notes:

[1] - Single group analysis.

Secondary: 2-year progression-free survival

End point title	2-year progression-free survival

End point description:

2-year progression-free survival as estimated by the Kaplan-Meier method

End point type	Secondary

End point timeframe:

From registration to two years after registration

End point values	Copanlisib + Obinutuzumab			
Subject group type	Reporting group			
Number of subjects analysed	100[2]			
Units: subjects				
number (confidence interval 95%)	0.74 (0.66 to 0.83)			

Notes:

[2] - Two patients did not have a censoring date for PFS.

Statistical analyses

No statistical analyses for this end point

Secondary: 1-year overall survival

End point title	1-year overall survival

End point description:

One-year overall survival as estimated by the Kaplan-Meier method

End point type	Secondary

End point timeframe:

From registration to one year after registration

End point values	Copanlisib + Obinutuzumab			
Subject group type	Reporting group			
Number of subjects analysed	102			
Units: subjects				
number (confidence interval 95%)	0.97 (0.93 to 1.00)			

Statistical analyses

No statistical analyses for this end point

Secondary: 2-year overall survival

End point title	2-year overall survival

End point description:

Two-year overall survival as estimated by the Kaplan-Meier method

End point type	Secondary

End point timeframe:

From registration to two years after registration

End point values	Copanlisib + Obinutuzumab			
Subject group type	Reporting group			
Number of subjects analysed	102			
Units: subjects				
number (confidence interval 95%)	0.93 (0.88 to 0.98)			

Statistical analyses

No statistical analyses for this end point

Secondary: 1-year response duration

End point title	1-year response duration

End point description:

In patients with CR or PR at the end of induction, duration of response was measured from the end-of-induction visit to disease progression or death from any cause.

End point type	Secondary

End point timeframe:

From end of induction to 1 year after end of induction

End point values	Copanlisib + Obinutuzumab			
Subject group type	Reporting group			
Number of subjects analysed	85			
Units: subjects				
number (confidence interval 95%)	0.83 (0.76 to 0.92)			

Statistical analyses

No statistical analyses for this end point

Secondary: 2-year response duration

End point title	2-year response duration

End point description:

In patients with CR or PR at the end of induction, duration of response was measured from the end-of-induction visit to disease progression or death from any cause.

End point type	Secondary

End point timeframe:

From end of induction to 2 years after end of induction

End point values	Copanlisib + Obinutuzumab			
Subject group type	Reporting group			
Number of subjects analysed	85			
Units: subjects				
number (confidence interval 95%)	0.67 (0.58 to 0.78)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From registration to end of study	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	4.03
Reporting groups	
Reporting group title	Safety population
Reporting group description: All patients who received therapy with copanlisib or obinutuzumab	

Serious adverse events	Safety population		
Total subjects affected by serious adverse events			
subjects affected / exposed	72 / 100 (72.00%)		
number of deaths (all causes)	8		
number of deaths resulting from adverse events	5		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant melanoma			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Second primary malignancy			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hypertension			
subjects affected / exposed	11 / 100 (11.00%)		
occurrences causally related to treatment / all	47 / 48		
deaths causally related to treatment / all	0 / 0		
Subclavian vein thrombosis			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Ischaemia				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Fever				
subjects affected / exposed	9 / 100 (9.00%)			
occurrences causally related to treatment / all	5 / 10			
deaths causally related to treatment / all	0 / 0			
Inflammation				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General physical health deterioration				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Immune system disorders				
Hypersensitivity				
subjects affected / exposed	2 / 100 (2.00%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Cytokine release syndrome				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Pneumonitis				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumothorax				

subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumocystis jirovecii pneumonia				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			
Upper respiratory tract inflammation				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Chylothorax				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypoxia				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Pleural effusion				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Organising pneumonia				

subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Panic attack			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Completed suicide			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Depression			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Creatine kinase increased			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Creatine kinase MB increased			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Transaminases increased			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatic enzyme increased			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural			

complications				
Infusion related reaction				
subjects affected / exposed	3 / 100 (3.00%)			
occurrences causally related to treatment / all	5 / 5			
deaths causally related to treatment / all	0 / 0			
Urinary tract procedural complication				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Femur fracture				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Multiple fractures				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Muscle rupture				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Forearm fracture				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Myocardial infarction				
subjects affected / exposed	2 / 100 (2.00%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Sinus bradycardia				
subjects affected / exposed	2 / 100 (2.00%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			

Atrial fibrillation				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Tachycardia				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac failure				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Lacunar infarction				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Parkinson's disease				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Transient ischaemic attack				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Neurological symptom				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Formication				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Peripheral sensory neuropathy				

subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Optic ischaemic neuropathy			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	3 / 100 (3.00%)		
occurrences causally related to treatment / all	4 / 4		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal haemorrhage			
subjects affected / exposed	2 / 100 (2.00%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Colitis			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pancreatitis			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastritis			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Enteritis				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Abdominal pain				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Terminal ileitis				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Oesophagitis				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Cholestasis				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Angioedema				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urticaria				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Dermatitis				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			

Neutrophilic dermatosis			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Rash			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Calculus urinary			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Urinary retention			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Euthyroid sick syndrome			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Muscle twitching			
subjects affected / exposed	1 / 100 (1.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Rhabdomyolysis			

subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vertebral lesion				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Spinal stenosis				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Lung infection				
subjects affected / exposed	15 / 100 (15.00%)			
occurrences causally related to treatment / all	8 / 19			
deaths causally related to treatment / all	0 / 0			
COVID-19				
subjects affected / exposed	10 / 100 (10.00%)			
occurrences causally related to treatment / all	2 / 11			
deaths causally related to treatment / all	0 / 2			
Urinary tract infection				
subjects affected / exposed	3 / 100 (3.00%)			
occurrences causally related to treatment / all	2 / 4			
deaths causally related to treatment / all	0 / 0			
Infections and infestations - other				
subjects affected / exposed	3 / 100 (3.00%)			
occurrences causally related to treatment / all	3 / 3			
deaths causally related to treatment / all	0 / 0			
Severe acute respiratory syndrome				
subjects affected / exposed	2 / 100 (2.00%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Sepsis				

subjects affected / exposed	2 / 100 (2.00%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Bacterial sepsis				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Oesophageal candidiasis				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis clostridial				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Encephalitis				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Superinfection bacterial				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Wound infection				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Atypical pneumonia				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Tooth infection				

subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Enterocolitis infectious				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory tract infection				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Endocarditis				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Erysipelas				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Herpes zoster				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Febrile infection				
subjects affected / exposed	1 / 100 (1.00%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Hyperglycaemia				
subjects affected / exposed	8 / 100 (8.00%)			
occurrences causally related to treatment / all	9 / 9			
deaths causally related to treatment / all	0 / 0			
Tumour lysis syndrome				

subjects affected / exposed	4 / 100 (4.00%)		
occurrences causally related to treatment / all	4 / 4		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Safety population		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	99 / 100 (99.00%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	50 / 100 (50.00%)		
occurrences (all)	293		
Thrombophlebitis			
subjects affected / exposed	6 / 100 (6.00%)		
occurrences (all)	6		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	28 / 100 (28.00%)		
occurrences (all)	33		
Pyrexia			
subjects affected / exposed	23 / 100 (23.00%)		
occurrences (all)	28		
Chills			
subjects affected / exposed	11 / 100 (11.00%)		
occurrences (all)	11		
Mucosal inflammation			
subjects affected / exposed	9 / 100 (9.00%)		
occurrences (all)	13		
Pain			
subjects affected / exposed	8 / 100 (8.00%)		
occurrences (all)	8		
Oedema peripheral			
subjects affected / exposed	7 / 100 (7.00%)		
occurrences (all)	8		
Chest discomfort			

subjects affected / exposed occurrences (all)	5 / 100 (5.00%) 5		
Immune system disorders Hypersensitivity subjects affected / exposed occurrences (all)	 8 / 100 (8.00%) 8		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Dyspnoea subjects affected / exposed occurrences (all)	 26 / 100 (26.00%) 28 8 / 100 (8.00%) 9		
Investigations C-reactive protein increased subjects affected / exposed occurrences (all) Blood lactate dehydrogenase increased subjects affected / exposed occurrences (all) Weight decreased subjects affected / exposed occurrences (all) Alanine aminotransferase increased subjects affected / exposed occurrences (all) Aspartate aminotransferase increased subjects affected / exposed occurrences (all) Gamma-glutamyltransferase increased subjects affected / exposed occurrences (all)	 8 / 100 (8.00%) 9 8 / 100 (8.00%) 12 7 / 100 (7.00%) 8 6 / 100 (6.00%) 9 6 / 100 (6.00%) 8 6 / 100 (6.00%) 7		
Cardiac disorders			

Tachycardia subjects affected / exposed occurrences (all)	5 / 100 (5.00%) 9		
Nervous system disorders Headache subjects affected / exposed occurrences (all) Peripheral sensory neuropathy subjects affected / exposed occurrences (all) Paraesthesia subjects affected / exposed occurrences (all)	 18 / 100 (18.00%) 23 7 / 100 (7.00%) 7 5 / 100 (5.00%) 5		
Blood and lymphatic system disorders Neutrophil count decreased subjects affected / exposed occurrences (all) Anaemia subjects affected / exposed occurrences (all) White blood cell count decreased subjects affected / exposed occurrences (all) Platelet count decreased subjects affected / exposed occurrences (all)	 22 / 100 (22.00%) 37 9 / 100 (9.00%) 14 7 / 100 (7.00%) 15 6 / 100 (6.00%) 9		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all) Constipation	 27 / 100 (27.00%) 58 19 / 100 (19.00%) 22 15 / 100 (15.00%) 31		

subjects affected / exposed	11 / 100 (11.00%)		
occurrences (all)	11		
Dyspepsia			
subjects affected / exposed	8 / 100 (8.00%)		
occurrences (all)	9		
Gastritis			
subjects affected / exposed	6 / 100 (6.00%)		
occurrences (all)	7		
Mucosal inflammation	Additional description: Stomatitis, aphthous stomatitis and aphthous ulcer were summarized		
subjects affected / exposed	6 / 100 (6.00%)		
occurrences (all)	9		
Vomiting			
subjects affected / exposed	6 / 100 (6.00%)		
occurrences (all)	6		
Dry mouth			
subjects affected / exposed	5 / 100 (5.00%)		
occurrences (all)	5		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	37 / 100 (37.00%)		
occurrences (all)	58		
Pruritus			
subjects affected / exposed	11 / 100 (11.00%)		
occurrences (all)	19		
Erythema			
subjects affected / exposed	8 / 100 (8.00%)		
occurrences (all)	8		
Night sweats			
subjects affected / exposed	6 / 100 (6.00%)		
occurrences (all)	7		
Eczema			
subjects affected / exposed	6 / 100 (6.00%)		
occurrences (all)	7		
Alopecia			

subjects affected / exposed	5 / 100 (5.00%)		
occurrences (all)	5		
Dry skin			
subjects affected / exposed	5 / 100 (5.00%)		
occurrences (all)	5		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	6 / 100 (6.00%)		
occurrences (all)	7		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	9 / 100 (9.00%)		
occurrences (all)	11		
Arthralgia			
subjects affected / exposed	9 / 100 (9.00%)		
occurrences (all)	12		
Myalgia			
subjects affected / exposed	7 / 100 (7.00%)		
occurrences (all)	7		
Pain in extremity			
subjects affected / exposed	6 / 100 (6.00%)		
occurrences (all)	7		
Neck pain			
subjects affected / exposed	5 / 100 (5.00%)		
occurrences (all)	5		
Infections and infestations			
COVID-19			
subjects affected / exposed	48 / 100 (48.00%)		
occurrences (all)	64		
Upper respiratory tract inflammation	Additional description: Upper respiratory tract inflammation and infection were summarized		
subjects affected / exposed	24 / 100 (24.00%)		
occurrences (all)	36		
Urinary tract infection			
subjects affected / exposed	13 / 100 (13.00%)		
occurrences (all)	13		
Bronchitis			

subjects affected / exposed occurrences (all)	11 / 100 (11.00%) 14		
Conjunctivitis subjects affected / exposed occurrences (all)	9 / 100 (9.00%) 12		
Pneumonia subjects affected / exposed occurrences (all)	6 / 100 (6.00%) 7		
Severe acute respiratory syndrome subjects affected / exposed occurrences (all)	6 / 100 (6.00%) 7		
Infections and infestations - other subjects affected / exposed occurrences (all)	6 / 100 (6.00%) 6		
Metabolism and nutrition disorders			
Hyperglycaemia subjects affected / exposed occurrences (all)	47 / 100 (47.00%) 313		
Vitamin D deficiency subjects affected / exposed occurrences (all)	6 / 100 (6.00%) 6		
Hyperkalaemia subjects affected / exposed occurrences (all)	5 / 100 (5.00%) 7		
Hypokalaemia subjects affected / exposed occurrences (all)	5 / 100 (5.00%) 5		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported