

**Clinical trial results:****A Phase 1/2 Proof-of-Concept Study of the Combination of Acalabrutinib and Vistusertib in Subjects with Relapsed/Refractory B-cell Malignancies****Summary**

EudraCT number	2016-003736-21
Trial protocol	GB
Global end of trial date	16 October 2018

Results information

Result version number	v1 (current)
This version publication date	05 December 2020
First version publication date	05 December 2020

Trial information**Trial identification**

Sponsor protocol code	ACE-LY-110
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Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Acerta Pharma B.V.
Sponsor organisation address	121 Oyster Point Boulevard, South San Francisco, United States, 94080
Public contact	Acerta Clinical Trials, Acerta Pharma B.V., +1 18882929613, acertamc@dls.com
Scientific contact	Acerta Clinical Trials, Acerta Pharma B.V., +1 18882929613, acertamc@dls.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	14 May 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 October 2018
Global end of trial reached?	Yes
Global end of trial date	16 October 2018
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To determine a dose and schedule for vistusertib in combination with acalabrutinib 100 mg bid, for evaluation of the safety of acalabrutinib and vistusertib when coadministered.

Protection of trial subjects:

The conduct of this clinical study met all local and regulatory requirements. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and are consistent with International Conference on Harmonization guideline: Good Clinical Practice, and applicable regulatory requirements. Participants signed an informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 September 2017
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	United States: 14
Country: Number of subjects enrolled	United Kingdom: 11
Worldwide total number of subjects	25
EEA total number of subjects	11

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)	9

From 65 to 84 years	15
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Adult subjects with a diagnosis of relapsed/refractory DLBCL as documented by medical records, who have no curative option with conventional therapy, and with at least 1 prior treatment with combination chemoimmunotherapy.

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?	Yes
Arm title	Acalabrutinib 100 mg BID plus Vistusertib BID Continuous

Arm description:

Continuous

Arm type	Experimental
Investigational medicinal product name	acalabrutinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

100 mg BID

Investigational medicinal product name	vistusertib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

BID continuous

Arm title	Acalabrutinib 100 mg BID plus Vistusertib BID Intermittent
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Arm description:

Intermittent

Arm type	Experimental
Investigational medicinal product name	vistusertib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

BID intermittent

Investigational medicinal product name	acalabrutinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule

Routes of administration	Oral use
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Dosage and administration details:

100 mg BID

Number of subjects in period 1	Acalabrutinib 100 mg BID plus Vistusertib BID Continuous	Acalabrutinib 100 mg BID plus Vistusertib BID Intermittent
Started	13	12
Completed	0	2
Not completed	13	10
Consent withdrawn by subject	1	2
Death	10	6
Study terminated by sponsor	2	1
Lost to follow-up	-	1

Baseline characteristics

Reporting groups

Reporting group title	Acalabrutinib 100 mg BID plus Vistusertib BID Continuous
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Reporting group description:

Continuous

Reporting group title	Acalabrutinib 100 mg BID plus Vistusertib BID Intermittent
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Reporting group description:

Intermittent

Reporting group values	Acalabrutinib 100 mg BID plus Vistusertib BID Continuous	Acalabrutinib 100 mg BID plus Vistusertib BID Intermittent	Total
Number of subjects	13	12	25
Age categorical			
Units: Subjects			
Adults (between 18 and 64)	5	4	9
>=65	8	8	16
Age Continuous			
Units: Years			
arithmetic mean	63.6	67.3	-
standard deviation	± 15.9	± 12.0	-
Sex: Female, Male			
Units:			
Male	9	10	19
Female	4	2	6
Region of Enrollment			
Units: Subjects			
United States	5	9	14
United Kingdom	8	3	11
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	0	1	1
Not Hispanic or Latino	11	11	22
Unknown or Not Reported	2	0	2
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	0	1
White	12	11	23
More than one race	0	0	0
Unknown or Not Reported	0	1	1

Subject analysis sets

Subject analysis set title	Acalabrutinib 100 mg BID* plus Vistusertib BID* Continuous
Subject analysis set type	Safety analysis
Subject analysis set description: Continuous	
Subject analysis set title	Acalabrutinib 100 mg BID* plus Vistusertib BID* Intermittent
Subject analysis set type	Safety analysis
Subject analysis set description: Intermittent	

Reporting group values	Acalabrutinib 100 mg BID* plus Vistusertib BID* Continuous	Acalabrutinib 100 mg BID* plus Vistusertib BID* Intermittent	
Number of subjects	13	12	
Age categorical Units: Subjects			
Adults (between 18 and 64)	5	4	
>=65	8	8	
Age Continuous Units: Years			
arithmetic mean	63.6	67.3	
standard deviation	± 15.9	± 12.0	
Sex: Female, Male Units:			
Male	9	10	
Female	4	2	
Region of Enrollment Units: Subjects			
United States	5	9	
United Kingdom	8	3	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	0	1	
Not Hispanic or Latino	11	11	
Unknown or Not Reported	2	0	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	0	0	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	1	0	
White	12	11	
More than one race	0	0	
Unknown or Not Reported	0	1	

End points

End points reporting groups

Reporting group title	Acalabrutinib 100 mg BID plus Vistusertib BID Continuous
Reporting group description:	Continuous
Reporting group title	Acalabrutinib 100 mg BID plus Vistusertib BID Intermittent
Reporting group description:	Intermittent
Subject analysis set title	Acalabrutinib 100 mg BID* plus Vistusertib BID* Continuous
Subject analysis set type	Safety analysis
Subject analysis set description:	Continuous
Subject analysis set title	Acalabrutinib 100 mg BID* plus Vistusertib BID* Intermittent
Subject analysis set type	Safety analysis
Subject analysis set description:	Intermittent

Primary: Number of Participants With Treatment-Emergent Adverse Events (AEs)

End point title	Number of Participants With Treatment-Emergent Adverse Events (AEs) ^[1]
End point description:	Safety assessments comprised type, frequency, severity, and relationship to either or both study drug of any AEs or abnormalities of laboratory tests; serious adverse events (SAEs); dose-limiting toxicities (DLTs); or AEs that led to dose modification, dose delay, or discontinuation of study drug(s).
End point type	Primary
End point timeframe:	From enrollment through up to 12 cycles of treatment

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: Descriptive statistics were used; there is no p value.

End point values	Acalabrutinib 100 mg BID* plus Vistusertib BID* Continuous	Acalabrutinib 100 mg BID* plus Vistusertib BID* Intermittent		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	13	12		
Units: Participants	13	12		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug until 30 days post last dose

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	21.1
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Reporting groups

Reporting group title	Acalabrutinib 100 mg BID plus Vistusertib BID Continuous
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Reporting group description:

Continuous

Reporting group title	Acalabrutinib 100 mg BID plus Vistusertib BID Intermittent
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Reporting group description:

Intermittent

Serious adverse events	Acalabrutinib 100 mg BID plus Vistusertib BID Continuous	Acalabrutinib 100 mg BID plus Vistusertib BID Intermittent	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 13 (15.38%)	6 / 12 (50.00%)	
number of deaths (all causes)	2	3	
number of deaths resulting from adverse events	0	0	
Investigations			
Computerised tomogram thorax abnormal			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Trigeminal neuralgia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	0 / 13 (0.00%)	2 / 12 (16.67%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymph node pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
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 / 13 (7.69%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Hypoxia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Cellulitis			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			

subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 13 (0.00%)	2 / 12 (16.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Acalabrutinib 100 mg BID plus Vistusertib BID Continuous	Acalabrutinib 100 mg BID plus Vistusertib BID Intermittent	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 13 (100.00%)	12 / 12 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour ulceration			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 13 (0.00%)	5 / 12 (41.67%)	
occurrences (all)	0	6	
Orthostatic hypotension			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Peripheral ischaemia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Chest pain			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	

Chills			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Fatigue			
subjects affected / exposed	4 / 13 (30.77%)	8 / 12 (66.67%)	
occurrences (all)	4	10	
Influenza like illness			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Injection site bruising			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Mucosal inflammation			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Non-cardiac chest pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Oedema			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Oedema peripheral			
subjects affected / exposed	1 / 13 (7.69%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Peripheral swelling			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Pyrexia			
subjects affected / exposed	2 / 13 (15.38%)	2 / 12 (16.67%)	
occurrences (all)	2	4	
Immune system disorders			
Seasonal allergy			

subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 12 (8.33%) 1	
Reproductive system and breast disorders Breast mass subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 12 (8.33%) 1	
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	2 / 13 (15.38%) 2	4 / 12 (33.33%) 4	
Dysphonia subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 12 (8.33%) 1	
Dyspnoea subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	2 / 12 (16.67%) 2	
Dyspnoea exertional subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 12 (8.33%) 1	
Hypoxia subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 12 (8.33%) 1	
Increased bronchial secretion subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 12 (0.00%) 0	
Nasal congestion subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 12 (0.00%) 0	
Oropharyngeal pain subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 12 (8.33%) 1	
Pleural effusion subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	1 / 12 (8.33%) 1	
Pneumonitis			

subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 12 (8.33%) 1	
Sinus congestion subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 12 (8.33%) 1	
Psychiatric disorders			
Agitation subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 12 (0.00%) 0	
Anxiety subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 12 (8.33%) 1	
Confusional state subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	3 / 12 (25.00%) 3	
Depressed mood subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 12 (0.00%) 0	
Insomnia subjects affected / exposed occurrences (all)	3 / 13 (23.08%) 3	0 / 12 (0.00%) 0	
Investigations			
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	1 / 12 (8.33%) 1	
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 12 (0.00%) 0	
Bacterial test positive subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 12 (8.33%) 1	
Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	1 / 12 (8.33%) 1	
Blood creatinine increased			

subjects affected / exposed occurrences (all)	4 / 13 (30.77%) 5	7 / 12 (58.33%) 11	
Blood urea increased subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 12 (8.33%) 1	
Ejection fraction decreased subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 12 (8.33%) 1	
Haemoglobin decreased subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 12 (0.00%) 0	
Lymphocyte count decreased subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 12 (8.33%) 3	
Platelet count decreased subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	1 / 12 (8.33%) 3	
Weight decreased subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	3 / 12 (25.00%) 3	
Electrocardiogram QT prolonged subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	2 / 12 (16.67%) 2	
Electrocardiogram T wave abnormal subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 12 (8.33%) 1	
Injury, poisoning and procedural complications Fall subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 12 (8.33%) 1	
Cardiac disorders Tachycardia subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 12 (8.33%) 1	
Nervous system disorders			

Disturbance in attention subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 12 (8.33%) 1	
Dizziness subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 12 (8.33%) 1	
Dysgeusia subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 12 (8.33%) 1	
Headache subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	4 / 12 (33.33%) 6	
Neuralgia subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	2 / 12 (16.67%) 2	
Neuropathy peripheral subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 12 (0.00%) 0	
Paraesthesia subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 12 (8.33%) 1	
Peripheral sensory neuropathy subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 12 (8.33%) 1	
Presyncope subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 12 (8.33%) 1	
Trigeminal neuralgia subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 12 (8.33%) 1	
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed occurrences (all)	2 / 13 (15.38%) 2	5 / 12 (41.67%) 7	
Increased tendency to bruise			

subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 12 (8.33%) 1	
Leukopenia subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	2 / 12 (16.67%) 7	
Lymphopenia subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 12 (8.33%) 1	
Neutropenia subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	2 / 12 (16.67%) 3	
Thrombocytopenia subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	3 / 12 (25.00%) 13	
Eye disorders Periorbital oedema subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 12 (8.33%) 1	
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	2 / 12 (16.67%) 2	
Abdominal pain upper subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 12 (0.00%) 0	
Aphthous ulcer subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 12 (8.33%) 1	
Constipation subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	6 / 12 (50.00%) 7	
Dry mouth subjects affected / exposed occurrences (all)	2 / 13 (15.38%) 2	4 / 12 (33.33%) 4	
Diarrhoea			

subjects affected / exposed occurrences (all)	6 / 13 (46.15%) 8	2 / 12 (16.67%) 5	
Dysphagia subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 12 (8.33%) 1	
Gastroesophageal reflux disease subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	2 / 12 (16.67%) 2	
Nausea subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	8 / 12 (66.67%) 10	
Stomatitis subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 12 (8.33%) 1	
Vomiting subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 2	5 / 12 (41.67%) 6	
Skin and subcutaneous tissue disorders			
Decubitus ulcer subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 12 (8.33%) 1	
Dermatitis subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 12 (8.33%) 2	
Erythema subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1	0 / 12 (0.00%) 0	
Pruritus subjects affected / exposed occurrences (all)	3 / 13 (23.08%) 3	2 / 12 (16.67%) 2	
Rash subjects affected / exposed occurrences (all)	3 / 13 (23.08%) 3	2 / 12 (16.67%) 4	
Rash maculo-papular subjects affected / exposed occurrences (all)	0 / 13 (0.00%) 0	1 / 12 (8.33%) 1	

Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 13 (7.69%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Chronic kidney disease			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Pollakiuria			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Back pain			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Joint swelling			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Muscle spasms			
subjects affected / exposed	1 / 13 (7.69%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 13 (0.00%)	2 / 12 (16.67%)	
occurrences (all)	0	2	
Myalgia			
subjects affected / exposed	2 / 13 (15.38%)	3 / 12 (25.00%)	
occurrences (all)	3	3	
Infections and infestations			
Candida infection			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Cellulitis			
subjects affected / exposed	2 / 13 (15.38%)	0 / 12 (0.00%)	
occurrences (all)	2	0	

Enterovirus infection			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Lower respiratory tract infection			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Nasopharyngitis			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Herpes zoster			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Oral candidiasis			
subjects affected / exposed	1 / 13 (7.69%)	1 / 12 (8.33%)	
occurrences (all)	1	1	
Pneumonia			
subjects affected / exposed	1 / 13 (7.69%)	2 / 12 (16.67%)	
occurrences (all)	1	3	
Respiratory tract infection			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Rhinovirus infection			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Sinusitis bacterial			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Tooth infection			
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)	
occurrences (all)	0	1	
Urinary tract infection			
subjects affected / exposed	1 / 13 (7.69%)	0 / 12 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	0 / 13 (0.00%)	6 / 12 (50.00%)
occurrences (all)	0	6
Dehydration		
subjects affected / exposed	0 / 13 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	3
Hypercalcaemia		
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	4
Hyperglycaemia		
subjects affected / exposed	3 / 13 (23.08%)	5 / 12 (41.67%)
occurrences (all)	5	7
Hypoalbuminaemia		
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	5
Hypoglycaemia		
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	1
Hypokalaemia		
subjects affected / exposed	2 / 13 (15.38%)	2 / 12 (16.67%)
occurrences (all)	2	2
Hypomagnesaemia		
subjects affected / exposed	0 / 13 (0.00%)	1 / 12 (8.33%)
occurrences (all)	0	1
Hyponatraemia		
subjects affected / exposed	0 / 13 (0.00%)	3 / 12 (25.00%)
occurrences (all)	0	4
Hypophosphataemia		
subjects affected / exposed	0 / 13 (0.00%)	2 / 12 (16.67%)
occurrences (all)	0	5

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 March 2017	Amendment 1
06 February 2018	Amendment 2

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
21 May 2018	study terminated by sponsor	-

Notes:

Limitations and caveats

None reported