Clinical trial results:
A Phase II Study of Pazopanib in Metastatic Merkel Cell Carcinoma

Summary

EudraCT number	2011-003226-27
Trial protocol	GB
Global end of trial date	08 July 2021

Results information

Result version number	v1 (current)
This version publication date	09 April 2026
First version publication date	09 April 2026

Trial information

Trial identification

Sponsor protocol code	RG_10-151

Additional study identifiers

ISRCTN number	ISRCTN10125877
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	CRCTU No: SK2006, SAF: ERN_11-1282, CTA Number: 21761/0277/001-0001, REC No.: 12/NW/0514, EudraCT No.: 2011-003226-27

Notes:

Sponsors

Sponsor organisation name	University of Birmingham
Sponsor organisation address	Edgbaston, Birmingham, United Kingdom, B15 2TT
Public contact	UKMCC-01 Trial Coordinator, University of Birmingham, 44 0121 414 3057, UKMCC-01@trials.bham.ac.uk
Scientific contact	UKMCC-01 Trial Coordinator, University of Birmingham, 44 0121 414 3057, UKMCC-01@trials.bham.ac.uk

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	03 July 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	09 November 2016
Global end of trial reached?	Yes
Global end of trial date	08 July 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objective of the UKMCC-01 study is to find out whether treatment with a drug called pazopanib is beneficial for patients with advanced MCC and thus warrants further investigation in a large, randomised, phase III trial. Advanced MCC patients have a poor prognosis and new treatment options for this group are desperately needed.
To assess whether pazopanib works we will determine the number of patients whose tumours disappear or reduce in size during treatment (technically called Clinical Response Rate).

Protection of trial subjects:

At each visit during the treatment period, patients were evaluated for the occurrence of AEs and laboratory abnormalities.
Dose reduction to a minimum of 400mg once daily to aid management of AEs was allowed.
Patients on pazopanib may have dose interruptions for up to 3 weeks (21 days) to recover from treatment emergent side effects.

Dose modification algorithms were presented to sites for potential treatment-related adverse events:
Hypertension
Proteinuria
Haemorrhage/Bleeding
Venous Thrombosis
Arterial Thrombosis
Thrombocytopenia
Anaemia
Other Clinically Significant Adverse events (graded 1-4)
Prolongation of QTc Interval

Recommendations for pazopanib dose interruptions/modifications in case of liver-related treatment-emergent AEs were also provided to sites.

Patient's were to discontinue study medication if necessary.

Background therapy:

N/A

Evidence for comparator:

No comparator in the trial as this is a single-arm phase II clinical trial.

Actual start date of recruitment	01 August 2012
Long term follow-up planned	Yes
Long term follow-up rationale	Scientific research
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 18
Worldwide total number of subjects	18
EEA total number of subjects	0

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)	5
From 65 to 84 years	12
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

The first patient was recruited into the trial on 28-Jan-2013 and the last patient 09-Feb-2016 (>2 years). All patients were recruited from hospitals within the UK. 18 patients were entered into the trial and an additional 4 were only registered.

Pre-assignment

Screening details:

Potential patients were identified via clinic referrals and Multi-disciplinary team meetings. The majority of screening tests were standard practice and were commenced prior to obtaining consent. Additional tests included: Electrocardiogram (ECG)

Period 1

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

Blinding implementation details:

N/A

Arms

Arm title	Intervention

Arm description:

Pazopanib (VotrientTM) is a multi-targeted oral kinase inhibitor licensed by the European Medicines Agency and by the Food and Drug Administration for use in renal cell carcinoma. Merkel Cell Carcinoma (MCC) is not a licensed indication for this drug. Although many patients with MCC are elderly there is no reason to consider that the safety profile in the MCC population will be significantly different from that seen in the renal cell carcinoma. Pazopanib is considered an Investigational Medicinal Product (IMP) for the UKMCC-01 trial.

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

Dosage and administration details:

Pazopanib (VotrientTM) is a multi-targeted oral kinase inhibitor. Pazopanib monohydrochloride is supplied as a series of aqueous film-coated tablets containing 200 mg of the freebase. The recommended dose of pazopanib is 800 mg per day, orally, continuous dosing. Pazopanib 800 mg (4 x 200 mg tablets) to be taken once daily by mouth. Treatment will continue until disease progression. For patients with concerns about tolerability but fulfil eligibility criteria, a starting dose of 600mg of pazopanib is permitted. If patients tolerate this dose and no toxicity is observed, the dose can be increased to 800mg.

Pazopanib taken orally one hour before or two hours after a meal. Tablets should be swallowed whole and not be crushed or broken. If dose is missed, the patient should take the dose as soon as possible, but not if there are less than 12 hours before the next dose is due. If the next dose is due in less than 12 hours, skip the missed dose and take the next dose as scheduled.

Number of subjects in period 1	Intervention
Started	18
Completed	18

Period 2

Period 2 title	End of Trial Outcome
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Intervention

Arm description:

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Pazopanib taken orally one hour before or two hours after a meal. Tablets should be swallowed whole and not be crushed or broken. If dose is missed, the patient should take the dose as soon as possible, but not if there are less than 12 hours before the next dose is due. If the next dose is due in less than 12 hours, skip the missed dose and take the next dose as scheduled.

Number of subjects in period 2	Intervention
Started	18
Completed	18

Baseline characteristics

Reporting groups	
Reporting group title	Baseline

Reporting group description: -

Reporting group values	Baseline	Total	
Number of subjects	18	18	
Age categorical Units: Subjects			
Adults (18-64 years)	5	5	
From 65-84 years	12	12	
85 years and over	1	1	
Age continuous Units: years			
median	72		
inter-quartile range (Q1-Q3)	63 to 81	-	
Gender categorical Units: Subjects			
Female	7	7	
Male	11	11	
ECOG Performance Status Units: Subjects			
PS0	5	5	
PS1	11	11	
PS2	1	1	
Not known	1	1	
Stage at presentation Units: Subjects			
0/IA	4	4	
IIA	1	1	
IIB	1	1	
IIIB	3	3	
IV	7	7	
Not known	2	2	
Disease Status Units: Subjects			
Unresectable Primary	2	2	
Unresectable regional lymph nodes	2	2	
Distant metastases	14	14	
Other cancer present Units: Subjects			
Cutaneous Basal Cell Carcinoma	1	1	
Cutaneous Squamous Cell Carcinoma	2	2	
None	15	15	
Site(s) of current disease Units: Subjects			
Skin and/or lymph nodes only	11	11	

Visceral metastases (liver, lung, muscle, adrenal)	7	7	
Prior Treatment - Surgery for Primary MCC Units: Subjects			
Received Surgery	12	12	
No Surgery	6	6	
Prior Treatment - Radiotherapy Units: Subjects			
Radiotherapy received	12	12	
No Radiotherapy	6	6	
Prior Treatment - Cytotoxic Chemotherapy Units: Subjects			
Cytotoxic Chemotherapy received	13	13	
No Cytotoxic Chemotherapy	5	5	
Height Units: metres			
median	1.7		
inter-quartile range (Q1-Q3)	1.6 to 1.8	-	
Weight Units: kg			
median	86.2		
inter-quartile range (Q1-Q3)	75.2 to 104.7	-	

End points

End points reporting groups

Reporting group title	Intervention

Reporting group description:

Pazopanib (VotrientTM) is a multi-targeted oral kinase inhibitor licensed by the European Medicines Agency and by the Food and Drug Administration for use in renal cell carcinoma. Merkel Cell Carcinoma (MCC) is not a licensed indication for this drug. Although many patients with MCC are elderly there is no reason to consider that the safety profile in the MCC population will be significantly different from that seen in the renal cell carcinoma. Pazopanib is considered an Investigational Medicinal Product (IMP) for the UKMCC-01 trial.

Reporting group title	Intervention

Reporting group description:

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Primary: Clinical Response Rate

End point title	Clinical Response Rate[1]

End point description:

Clinical Response Rate is defined as the proportion of patients with complete response (CR) or confirmed partial response (PR). Response will be determined using Response Evaluation Criteria in Solid Tumours (RECIST) version 1.1.
Results for CRR cannot be captured in statistical test so have added here for completeness. 3/18 patients, CRR = 17% (1-sided 85% LCI; 10)

End point type	Primary

End point timeframe:

CT scans are to be assessed by RECIST1.1 at every 8 weeks until progression. Patients can experience a complete or partial response at any time.

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: EudraCT FAQ explanation for reporting single-arm trials
"The statistical analysis for an endpoint is not mandatory. You could choose to delete the statistical analysis (go to the analysis page, scroll down, and select "delete statistical analysis"). This will generate a warning which you can reply to with a justification for not entering the analysis."
The statistical evaluation for this outcome is a CRR of 17% with a 1-sided 85% CI of 10.
The outcome DCR was 50% with 2-sided 95%; 29, 71.

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: patients				
Clinical Response Rate	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Disease Control Rate

End point title	Disease Control Rate

End point description:

DCR is defined as the percentage of patients who have stable disease, a PR, or a CR for more than 12 weeks.
Results for DCR cannot be captured in statistical test so have added here for completeness. 9/18 patients, DCR = 50% (2-sided 95% CI; 29; 71)

End point type	Secondary

End point timeframe:

DCR is assessed by CT Scan throughout the patient treatment plan until progression or death.

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: patients				
DCR	9			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression free survival time

End point title	Progression free survival time

End point description:

PFS: defined as the time from entry into the trial until disease progression or death from any cause. Patients not having died or progressed will be censored at the date last seen alive.

End point type	Secondary

End point timeframe:

Endpoint of the whole trial

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: months				
median (confidence interval 95%)	2.76 (1.45 to 5.22)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression-free Survival at 3 months

End point title	Progression-free Survival at 3 months

End point description:

PFS: defined as the time from entry into the trial until disease progression or death from any cause. Patients not having died or progressed will be censored at the date last seen alive.

End point type	Secondary

End point timeframe:

PFS at 3 months.

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: Survival Proportion				
number (confidence interval 95%)	0.49 (0.25 to 0.69)			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of response

End point title	Duration of response

End point description:

Duration of response: defined as the time from date of first response (partial or complete) to date of progression or death from any cause.

End point type	Secondary

End point timeframe:

Trial Endpoint

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: days				
number (not applicable)				
Response Duration 1	40			
Response Duration 2	77			
Response Duration 3	115			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival time

End point title	Overall survival time

End point description:

Overall survival defined as the time from entry into the trial until death from any cause. Patients will be censored at the date last seen alive. All patients will be followed up until death or for a maximum of 5 years.

End point type	Secondary

End point timeframe:

Trial Endpoint

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: months				
median (confidence interval 95%)	6.41 (3.91 to 13.17)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival time at 3 months

End point title	Overall survival time at 3 months

End point description:

Overall survival defined as the time from entry into the trial until death from any cause. Patients will be censored at the date last seen alive. All patients will be followed up until death or for a maximum of 5 years.

End point type	Secondary

End point timeframe:

Trial Endpoint

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: proportion				
number (confidence interval 95%)	0.83 (0.57 to 0.94)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Details of AEs were to be documented and reported from the date of consent until 28 days after the administration of the last dose of pazopanib. SAEs which meet the definition of a SUSAR should continue to be reported after this period.

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	4.0

Reporting groups

Reporting group title	Intervention

Reporting group description:

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Serious adverse events	Intervention		
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 18 (55.56%)		
number of deaths (all causes)	16		
number of deaths resulting from adverse events	0		
Investigations			
Raised LFTs			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Hematoma			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Thromboembolic Event			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Cardiac disorders			

Cardiac dysfunction			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Syncope			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Malaise			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 1		
Respiratory, thoracic and mediastinal disorders			
Bronchopulmonary Hemorrhage			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Dyspnoea			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Hepatobiliary disorders			
Jaundice			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Renal and urinary disorders			

Renal Failure			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		

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

Non-serious adverse events	Intervention		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	18 / 18 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign Prostate Hypertrophy			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Tumour Pain			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	4		
Vascular disorders			
Hematoma			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Hypertension			
subjects affected / exposed	6 / 18 (33.33%)		
occurrences (all)	10		
Lymphedema			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	3		
Thromboembolic Event			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	4		
General disorders and administration site conditions			
Edema face			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Edema Limbs			

subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	3		
Fatigue			
subjects affected / exposed	17 / 18 (94.44%)		
occurrences (all)	100		
Flu Like Symptoms			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	2		
Localised Edema			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Malaise			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Pain			
subjects affected / exposed	5 / 18 (27.78%)		
occurrences (all)	8		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	6 / 18 (33.33%)		
occurrences (all)	7		
Dyspnoea			
subjects affected / exposed	8 / 18 (44.44%)		
occurrences (all)	22		
Sore Throat			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Voice Alteration			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	2		
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Blood Bilirubin Increased			

subjects affected / exposed occurrences (all)	5 / 18 (27.78%) 7		
Cholesterol High subjects affected / exposed occurrences (all)	2 / 18 (11.11%) 2		
Electrocardiogram Qt Corrected Interval Prolonged subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1		
Elevated LFTs and GGT subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1		
Lymphocyte Count Decreased subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 2		
Neutrophil Count Decreased subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 2		
Platelet Count Decreased subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 2		
Weight Loss subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 5		
White Blood Cell Decreased subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 2		
Injury, poisoning and procedural complications Bruising subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1		
Cardiac disorders Atrial Fibrillation subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 2		
Myocardial Infarction			

subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	3		
Dysgeusia			
subjects affected / exposed	3 / 18 (16.67%)		
occurrences (all)	4		
Headache			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Neuralgia			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	2		
Paresthesia			
subjects affected / exposed	3 / 18 (16.67%)		
occurrences (all)	27		
Phantom Pain			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Syncope			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	3 / 18 (16.67%)		
occurrences (all)	7		
Lymphadenopathy			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Eye disorders			
Deterioration of eyesight			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	2		
Eye pain			

subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Glaucoma			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Puffy eyes			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	5 / 18 (27.78%)		
occurrences (all)	11		
Ascites			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	3		
Constipation			
subjects affected / exposed	9 / 18 (50.00%)		
occurrences (all)	21		
Diarrhea			
subjects affected / exposed	8 / 18 (44.44%)		
occurrences (all)	56		
Dyspepsia			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	3		
Gastroesophageal Reflux Disease			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Oral Mucositis			
subjects affected / exposed	6 / 18 (33.33%)		
occurrences (all)	12		
Nausea			
subjects affected / exposed	12 / 18 (66.67%)		
occurrences (all)	30		
Oral Pain			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	3		

Vomiting			
subjects affected / exposed	4 / 18 (22.22%)		
occurrences (all)	7		
Hepatobiliary disorders			
Bile Duct Stenosis			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Raised LDH			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	7 / 18 (38.89%)		
occurrences (all)	14		
Dry Skin			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	3		
Palmar-Plantar Erythrodysesthesia Syndrome			
subjects affected / exposed	2 / 18 (11.11%)		
occurrences (all)	21		
Periorbital Edema			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Rash Acneform			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	5		
Skin Nodules on Abdomen			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	2		
Spots on Abdomen / In Axilla			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	1		
Ulcerating Skin Nodules on Abdomen			
subjects affected / exposed	1 / 18 (5.56%)		
occurrences (all)	2		
Urticaria			

subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 2		
Renal and urinary disorders Proteinuria subjects affected / exposed occurrences (all) Raised Urea subjects affected / exposed occurrences (all)	 2 / 18 (11.11%) 2 1 / 18 (5.56%) 1		
Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all)	 1 / 18 (5.56%) 1		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Arthritis subjects affected / exposed occurrences (all) Back Pain subjects affected / exposed occurrences (all) Pain in Extremity subjects affected / exposed occurrences (all)	 4 / 18 (22.22%) 11 1 / 18 (5.56%) 1 5 / 18 (27.78%) 17 6 / 18 (33.33%) 29		
Infections and infestations Biliary Tract Infection subjects affected / exposed occurrences (all) Lung Infection subjects affected / exposed occurrences (all) Mucosal infection subjects affected / exposed occurrences (all)	 1 / 18 (5.56%) 1 1 / 18 (5.56%) 1 2 / 18 (11.11%) 2		

Pharyngitis subjects affected / exposed occurrences (all) Skin infection subjects affected / exposed occurrences (all) Urinary Tract Infection subjects affected / exposed occurrences (all)	1 / 18 (5.56%) 1 3 / 18 (16.67%) 5 3 / 18 (16.67%) 5		
Metabolism and nutrition disorders Anorexia subjects affected / exposed occurrences (all) Dehydration subjects affected / exposed occurrences (all) Hyponatremia subjects affected / exposed occurrences (all)	10 / 18 (55.56%) 31 1 / 18 (5.56%) 1 1 / 18 (5.56%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 November 2013	Introduced additional LFT (Wk. 3) Change in eligibility criteria (INR & UPC/ACR ratio) Additional guidance on blood sample collection and CT scan timings Updated CRF Completion guidance Updated AST hepatotoxicity guidance Other minor amendments and corrections
25 October 2018	Change in Data Protection Regulations

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported