



Clinical trial results:

A phase II, open label study to investigate the efficacy and safety of domatinostat in combination with avelumab in patients with advanced unresectable/metastatic Merkel Cell Carcinoma progressing on anti-PD (L)1 antibody therapy – the MERKLIN 2 study

Summary

EudraCT number	2018-004788-30
Trial protocol	DE ES BE NL FR IT
Global end of trial date	26 February 2024

Results information

Result version number	v1 (current)
This version publication date	08 February 2025
First version publication date	08 February 2025

Trial information

Trial identification

Sponsor protocol code	4SC-202-3-2018
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04393753
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	4SC AG
Sponsor organisation address	Fraunhoferstr. 22, Planegg-Martinsried, Germany, 82152
Public contact	Corporate Communications, 4SC AG, 0049 897007630, public@4sc.com
Scientific contact	Clinical Operations, 4SC AG, 0049 897007630, MERKLIN2@4sc.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	20 March 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 February 2024
Global end of trial reached?	Yes
Global end of trial date	26 February 2024
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To investigate the anti-tumor efficacy of domatinostat in combination with avelumab in patients with advanced unresectable/metastatic Merkel cell carcinoma (MCC) progressing on anti-PD-(L)1 antibody monotherapy.

Protection of trial subjects:

An independent Safety Review Committee (SRC) was implemented to regularly review the safety data of the study. The SRC reviewed selected safety and other relevant data across the clinical study at regular, pre-defined intervals with special attention to the first patients treated in the clinical study to confirm the safety of the treatment regimen and to continuously reassess the risk-benefit ratio of the study treatment. The SRC was asked to make recommendations about overall safety aspects, as well as continuation, modification or termination of the clinical study for safety concerns. Additionally, after the first 6 patients were enrolled in the study and received domatinostat and 2 infusions of avelumab, the SRC reviewed the safety data for these patients and recommended either continuing the study at the same dose level or reducing the dose of domatinostat, in case safety issues were identified.

Before the start of a new treatment cycle, subjects were assessed including adverse events, physical examination, and measurement of hematological and biochemical parameters. Depending on the observed toxicities, the dose of domatinostat could be individually reduced by 50% of the total daily dose. Guidance was given in the study protocol concerning actions to be taken due to the observed toxicities (dose reduction, interruption, discontinuation). Subjects requiring more than one dose reduction had to be discontinued.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 October 2020
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	Netherlands: 1
Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	France: 5
Country: Number of subjects enrolled	Germany: 8
Country: Number of subjects enrolled	Italy: 4
Worldwide total number of subjects	19
EEA total number of subjects	19

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)	8
From 65 to 84 years	10
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Study participants were screened in 22 centers, in Belgium (1 center), France (4 centers), Germany (10 centers), Italy (4 centers), The Netherlands (2 centers), and Spain (1 center); 16 centers (1 in Belgium, 4 in France, 7 in Germany, 3 in Italy and 1 in the Netherlands) enrolled 19 patients in the study between 30-Oct-2020 and 23-Dec-2021.

Pre-assignment

Screening details:

Subjects were screened during a 28-day screening period, prior to the start of study drug. 30 subjects were screened from 13-Oct-2020 to 11-Jan-2022; 11 subjects were screening failures due to violation of inclusion or exclusion criteria (N=9), withdrawal of consent (N=1) or sponsor's decision (N=1).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1

Arm description:

Included subjects progressing on avelumab (anti-PD-L1 antibody).

Arm type	Experimental
Investigational medicinal product name	Domatinostat
Investigational medicinal product code	4SC-202
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Domatinostat was taken every day twice daily with a total daily dose of 400 mg/d, in fasting conditions (two hours prior and one hour after domatinostat intake) together with 200 mL of water.

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

Dosage and administration details:

Avelumab was given intravenously as a short-infusion over 60 minutes at a dose of 800 mg every 2 weeks corresponding to 4 vials each containing 200 mg avelumab.

Arm title	Cohort 2
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Arm description:

Included subjects progressing on any anti-PD-1 antibody.

Arm type	Experimental
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Investigational medicinal product name	Domatinostat
Investigational medicinal product code	4SC-202
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Domatinostat was taken every day twice daily with a total daily dose of 400 mg/d, in fasting conditions (two hours prior and one hour after domatinostat intake) together with 200 mL of water.

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

Dosage and administration details:

Avelumab was given intravenously as a short-infusion over 60 minutes at a dose of 800 mg every 2 weeks corresponding to 4 vials each containing 200 mg avelumab.

Number of subjects in period 1	Cohort 1	Cohort 2
Started	17	2
Completed	17	2

Baseline characteristics

Reporting groups

Reporting group title	Cohort 1
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Reporting group description:

Included subjects progressing on avelumab (anti-PD-L1 antibody).

Reporting group title	Cohort 2
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Reporting group description:

Included subjects progressing on any anti-PD-1 antibody.

Reporting group values	Cohort 1	Cohort 2	Total
Number of subjects	17	2	19
Age categorical			
Units: Subjects			
Adults (18-64 years)	6	2	8
From 65-84 years	10	0	10
85 years and over	1	0	1
Gender categorical			
Units: Subjects			
Female	3	1	4
Male	14	1	15

End points

End points reporting groups

Reporting group title	Cohort 1
Reporting group description:	
Included subjects progressing on avelumab (anti-PD-L1 antibody).	
Reporting group title	Cohort 2
Reporting group description:	
Included subjects progressing on any anti-PD-1 antibody.	
Subject analysis set title	Full Analysis Set
Subject analysis set type	Full analysis
Subject analysis set description:	
The Full Analysis Set (FAS) population includes all subjects who received at least one dose of study medication (domatinostat or avelumab).	

Primary: Objective Response Rate (ORR)

End point title	Objective Response Rate (ORR) ^[1]
End point description:	
Percentage of patients having a confirmed CR or PR according to RECIST v1.1. Assessment was done by radiological imaging and response evaluation according to RECIST v1.1 by the investigator. CT or MRI scans (CT preferred) were done every 8 weeks for the first 6 months and every 12 weeks thereafter. The same imaging technique as used at baseline/screening should be used throughout the study.	
End point type	Primary
End point timeframe:	
Entire study participation	

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: Study was discontinued prematurely. Therefore only descriptive analysis of the data was performed: categorical variables were summarized using frequency tables showing the number and percentage of patients within a particular category.

End point values	Cohort 1	Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	2		
Units: subjects				
Objective Response	1	0		
No Objective Response	16	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Disease Control Rate (DCR)

End point title	Disease Control Rate (DCR)
End point description:	
Proportion of patients with either an objective response (CR, PR) or stable disease (SD) according to RECIST v1.1.	

End point type	Secondary
End point timeframe:	
Entire study participation	

End point values	Cohort 1	Cohort 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	2		
Units: subjects				
Disease Control	7	0		
No Disease Control	10	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)
End point description:	
Time from first dosing (day 1) to the date of progressive disease or death from any cause (whichever comes first).	
End point type	Secondary
End point timeframe:	
From first dosing to progression or death	

End point values	Full Analysis Set			
Subject group type	Subject analysis set			
Number of subjects analysed	19			
Units: days				
number (confidence interval 95%)				
25% Quartile	51 (32 to 56)			
50% Quartile	58 (49 to 115)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The period of observation for collection of adverse events extended from signing informed consent form until 90 days after last administration of study treatment.

Adverse event reporting additional description:

At each visit, the investigator asked for well-being and AEs by using neutral and non-leading questions. Additionally, clinically significant changes from baseline physical examination or other safety assessments were recorded as AEs.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	23
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Reporting groups

Reporting group title	Cohort 1
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Reporting group description:

Subjects progressing on avelumab (anti-PD-L1 antibody)

Reporting group title	Cohort 2
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Reporting group description:

Subjects progressing on any anti-PD-1 antibody.

Serious adverse events	Cohort 1	Cohort 2	
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 17 (29.41%)	1 / 2 (50.00%)	
number of deaths (all causes)	5	2	
number of deaths resulting from adverse events	0	0	
General disorders and administration site conditions			
Pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	1 / 17 (5.88%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Immune-mediated hepatitis			

subjects affected / exposed	1 / 17 (5.88%)	0 / 2 (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 failure			
subjects affected / exposed	1 / 17 (5.88%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 17 (0.00%)	1 / 2 (50.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	0 / 17 (0.00%)	1 / 2 (50.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydronephrosis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Adenocorticotrophic hormone deficiency			
subjects affected / exposed	1 / 17 (5.88%)	0 / 2 (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			
Pain in extremity			
subjects affected / exposed	1 / 17 (5.88%)	0 / 2 (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			
Dermo-hypodermatitis			

subjects affected / exposed	0 / 17 (0.00%)	1 / 2 (50.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	1 / 17 (5.88%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Cohort 1	Cohort 2	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 17 (100.00%)	1 / 2 (50.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant ascites			
subjects affected / exposed	1 / 17 (5.88%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Skin papilloma			
subjects affected / exposed	1 / 17 (5.88%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Tumour pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 17 (5.88%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Asthenia			

subjects affected / exposed	4 / 17 (23.53%)	1 / 2 (50.00%)	
occurrences (all)	5	1	
Fatigue			
subjects affected / exposed	2 / 17 (11.76%)	0 / 2 (0.00%)	
occurrences (all)	9	0	
Impaired healing			
subjects affected / exposed	1 / 17 (5.88%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Mucosal inflammation			
subjects affected / exposed	1 / 17 (5.88%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Oedema peripheral			
subjects affected / exposed	1 / 17 (5.88%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Pyrexia			
subjects affected / exposed	1 / 17 (5.88%)	1 / 2 (50.00%)	
occurrences (all)	1	1	
Reproductive system and breast disorders			
Penile oedema			
subjects affected / exposed	1 / 17 (5.88%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Testicular oedema			
subjects affected / exposed	1 / 17 (5.88%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	4 / 17 (23.53%)	0 / 2 (0.00%)	
occurrences (all)	5	0	
Dyspnoea exertional			
subjects affected / exposed	2 / 17 (11.76%)	0 / 2 (0.00%)	
occurrences (all)	2	0	
Haemoptysis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Pneumonitis			

subjects affected / exposed	1 / 17 (5.88%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Rhinorrhoea			
subjects affected / exposed	1 / 17 (5.88%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 17 (5.88%)	1 / 2 (50.00%)	
occurrences (all)	1	1	
Insomnia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Sleep disorder			
subjects affected / exposed	1 / 17 (5.88%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 17 (11.76%)	0 / 2 (0.00%)	
occurrences (all)	2	0	
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 17 (11.76%)	0 / 2 (0.00%)	
occurrences (all)	2	0	
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Blood creatine phosphokinase increased			
subjects affected / exposed	2 / 17 (11.76%)	0 / 2 (0.00%)	
occurrences (all)	2	0	
Blood creatinine increased			
subjects affected / exposed	2 / 17 (11.76%)	0 / 2 (0.00%)	
occurrences (all)	3	0	
Blood urea increased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
C-reactive protein increased			

subjects affected / exposed	2 / 17 (11.76%)	0 / 2 (0.00%)	
occurrences (all)	2	0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	2 / 17 (11.76%)	0 / 2 (0.00%)	
occurrences (all)	3	0	
Glomerular filtration rate increased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Lipase increased			
subjects affected / exposed	1 / 17 (5.88%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Platelet count decreased			
subjects affected / exposed	2 / 17 (11.76%)	0 / 2 (0.00%)	
occurrences (all)	2	0	
Injury, poisoning and procedural complications			
Accidental overdose			
subjects affected / exposed	1 / 17 (5.88%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 17 (5.88%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Dysaesthesia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Dysgeusia			
subjects affected / exposed	2 / 17 (11.76%)	0 / 2 (0.00%)	
occurrences (all)	3	0	
Headache			
subjects affected / exposed	1 / 17 (5.88%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 17 (23.53%)	0 / 2 (0.00%)	
occurrences (all)	4	0	

Leukopenia			
subjects affected / exposed	2 / 17 (11.76%)	0 / 2 (0.00%)	
occurrences (all)	2	0	
Lymphadenectomy			
subjects affected / exposed	1 / 17 (5.88%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Lymphopenia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Thrombocytopenia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 2 (0.00%)	
occurrences (all)	3	0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	2 / 17 (11.76%)	0 / 2 (0.00%)	
occurrences (all)	2	0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 17 (11.76%)	0 / 2 (0.00%)	
occurrences (all)	3	0	
Constipation			
subjects affected / exposed	4 / 17 (23.53%)	1 / 2 (50.00%)	
occurrences (all)	4	1	
Diarrhoea			
subjects affected / exposed	6 / 17 (35.29%)	0 / 2 (0.00%)	
occurrences (all)	6	0	
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 17 (11.76%)	0 / 2 (0.00%)	
occurrences (all)	2	0	
Nausea			
subjects affected / exposed	5 / 17 (29.41%)	1 / 2 (50.00%)	
occurrences (all)	7	1	
Pancreatitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Periodontal disease			

subjects affected / exposed	1 / 17 (5.88%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	1 / 17 (5.88%)	1 / 2 (50.00%)	
occurrences (all)	3	1	
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	1 / 17 (5.88%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Papule			
subjects affected / exposed	1 / 17 (5.88%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Pruritus			
subjects affected / exposed	2 / 17 (11.76%)	0 / 2 (0.00%)	
occurrences (all)	2	0	
Rash			
subjects affected / exposed	1 / 17 (5.88%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Rash erythematous			
subjects affected / exposed	1 / 17 (5.88%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 17 (5.88%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Haematuria			
subjects affected / exposed	2 / 17 (11.76%)	0 / 2 (0.00%)	
occurrences (all)	2	0	
Hypertonic bladder			
subjects affected / exposed	1 / 17 (5.88%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Polyuria			
subjects affected / exposed	1 / 17 (5.88%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Urinary retention			

subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 2 (0.00%) 0	
Urinary tract obstruction subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 2 (0.00%) 0	
Endocrine disorders Hyperthyroidism subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 2	0 / 2 (0.00%) 0	
Hypothyroidism subjects affected / exposed occurrences (all)	2 / 17 (11.76%) 3	0 / 2 (0.00%) 0	
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 2 (0.00%) 0	
Pain in extremity subjects affected / exposed occurrences (all)	2 / 17 (11.76%) 2	0 / 2 (0.00%) 0	
Infections and infestations COVID-19 subjects affected / exposed occurrences (all)	2 / 17 (11.76%) 2	0 / 2 (0.00%) 0	
Diverticulitis subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 2 (0.00%) 0	
Herpes simplex subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 2 (0.00%) 0	
Localised infection subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 2 (0.00%) 0	
Tonsillitis bacterial subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 2 (0.00%) 0	
Urinary tract infection			

subjects affected / exposed occurrences (all)	3 / 17 (17.65%) 4	0 / 2 (0.00%) 0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	3 / 17 (17.65%)	0 / 2 (0.00%)	
occurrences (all)	5	0	
Hypoalbuminaemia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Hypocalcaemia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 2 (0.00%)	
occurrences (all)	1	0	
Hyponatraemia			
subjects affected / exposed	2 / 17 (11.76%)	0 / 2 (0.00%)	
occurrences (all)	2	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 March 2020	<ul style="list-style-type: none">• Introduction of additional safety information and toxicity management guidelines regarding the delayed hypersensitivity for combination of domatinostat with anti-PD-(L)1 antibodies• Updates to Schedule of Activities to clarify study timepoints• Other administrative changes to clarify wording in protocol• All tables in protocol numbered

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study was prematurely terminated based on a sponsor's data review of 2 ongoing clinical trials with domatinostat, concluding that it is very unlikely that domatinostat may provide significant benefit to these patients due to lack of efficacy.

Notes: