Clinical trial results:
A phase II trial assessing nivolumab in strong class II expressing microsatellite stable colorectal cancer

Summary

EudraCT number	2018-000318-39
Trial protocol	GB
Global end of trial date	27 November 2024

Results information

Result version number	v1 (current)
This version publication date	13 May 2026
First version publication date	13 May 2026

Trial information

Trial identification

Sponsor protocol code	RG_17-215

Additional study identifiers

ISRCTN number	ISRCTN40245896
ClinicalTrials.gov id (NCT number)	NCT03981146
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University of Birmingham
Sponsor organisation address	Edgbaston, Birmingham, United Kingdom, B15 2TT
Public contact	Joshua Savage, University of Birmingham, anicca-classII@trials.bham.ac.uk
Scientific contact	Joshua Savage, University of Birmingham, anicca-classII@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	14 February 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 November 2024
Global end of trial reached?	Yes
Global end of trial date	27 November 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this trial is to detect the rate of durable clinical benefit in patients with strong class II expressing Micro Satellite Stable Colorectal Cancer treated with single agent nivolumab, to justify further investigation in subsequent studies.

Protection of trial subjects:

The Trial Steering Committee (TSC) provides overall supervision for the trial on behalf of the Trial Sponsor (University of Birmingham) and to ensure that the trial is conducted to the rigorous standards set out in the GCP standards. In particular, the TSC will concentrate on progress of the trial, adherence to the protocol, patient safety, evidence on main efficacy outcome measures and the consideration of new information of relevance to the research question. The safety and well-being of the trial participants are the most important considerations and should prevail over the interests of science and society. The TSC will provide advice, through its Chair, to the Chief Investigator and the University of Birmingham on all appropriate aspects of the trial. Membership of the TSC includes an independent Chair and two other independent members, who do not sit on the TMG, including a Patient, Public & Involvement (PPI) representative. The TSC will be asked to comment in detail on substantial changes to the protocol. The TSC will meet as often as required, at least once per year during recruitment.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 August 2019
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	United Kingdom: 35
Worldwide total number of subjects	35
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)	23
From 65 to 84 years	12
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The trial opened to recruitment on 28th August 2019 with the first patient screened on 4th September 2019 and the first patient registered on 3rd August 2020. The last patient was recruited on 5th August 2021 and the trial closed to recruitment on 6th September 2021.

Pre-assignment

Screening details:

464 patients consented for determination of microsatellite (MSS) & class II status. 457 provided a screening biopsy for testing, which was performed centrally at Queen Elizabeth Hospital Birmingham (University Hospitals Birmingham NHS Foundation Trust). This was successful in 444 (97%) patients, 58 were confirmed to have MSS class II expression.

Period 1

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

Arms

Arm title	Nivolumab

Arm description:

Nivolumab will be administered as a 60 minute IV infusion, with a window of -5 and +10 minutes, at a flat dose of 480mg. A dosing interval every 4 weeks (Q4W) was employed. Patients could receive nivolumab for a maximum of 2 years, or until disease progression, unacceptable toxicity or withdrawal of consent. With the first dose, cycle 1 day 1, to be given within 7 days of registration to the trial.

Arm type	Experimental
Investigational medicinal product name	Nivolumab
Investigational medicinal product code	
Other name	Opdivo
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Nivolumab was provided as vials containing 10 mg/mL concentrate of drug substance in solution for infusion. Administered as a 60 minute IV infusion, with a window of -5 and +10 minutes, at a flat dose of 480mg. A dosing interval every 4 weeks (Q4W) was employed. Patients could receive nivolumab for a maximum of 2 years, or until disease progression, unacceptable toxicity or withdrawal of consent. With the first dose, cycle 1 day 1, to be given within 7 days of registration to the trial.

Number of subjects in period 1	Nivolumab
Started	35
Completed	35

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	35	35	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	23	23	
From 65-84 years	12	12	
85 years and over	0	0	
Age continuous Units: years			
median	63		
full range (min-max)	37 to 81	-	
Gender categorical Units: Subjects			
Female	16	16	
Male	19	19	
Primary Cancer Stage Units: Subjects			
Ascending colon	4	4	
Descending colon	3	3	
Transverse colon	2	2	
Sigmoid colon	14	14	
Rectum	12	12	
Primary Resection Performed Units: Subjects			
No	7	7	
Yes	28	28	
RAS Mutations Units: Subjects			
KRAS	16	16	
NRAS	3	3	
BRAF	1	1	
Not Known	15	15	
ECOG Performance Status Units: Subjects			
PS 0	11	11	

PS 1	23	23	
Not Known	1	1	
Smoking Status Units: Subjects			
Never smoked	22	22	
Ex-smoker	12	12	
Current smoker	1	1	
Previous Lines of Therapy Units: Lines of Therapy			
median	6		
full range (min-max)	1 to 16	-	
Smoking Pack Years			
Pack years measure a person's cumulative exposure to cigarette smoke, calculated by multiplying the number of packs smoked per day by the number of years smoked. For example, Smoking 1 pack per day for 20 years equals 20 pack years.			
Units: Pack Years			
median	5		
full range (min-max)	0 to 16	-	
Smoking Stopped Years			
For ex-smokers, this is the number of years ago that the patient stopped smoking. This measure only applies to patients who are ex-smokers (12 patients), however, only 10 patients provided this data. Patients who never smoked or currently smoke are not included - see baseline characteristic "Smoking Status".			
Units: Years			
median	30		
full range (min-max)	4 to 50	-	

End points

End points reporting groups

Reporting group title	Nivolumab

Reporting group description:

Nivolumab will be administered as a 60 minute IV infusion, with a window of -5 and +10 minutes, at a flat dose of 480mg. A dosing interval every 4 weeks (Q4W) was employed. Patients could receive nivolumab for a maximum of 2 years, or until disease progression, unacceptable toxicity or withdrawal of consent. With the first dose, cycle 1 day 1, to be given within 7 days of registration to the trial.

Primary: Durable Clinical Benefit

End point title	Durable Clinical Benefit[1]

End point description:

Patient will be defined as experiencing DCB if they remain free of disease progression at their third trial specific CT scan since treatment start date (i.e. at approximately 27 weeks) or at any CT scan after 27 weeks that shows the patient remains free of disease progression

End point type	Primary

End point timeframe:

Beginning of trial treatment to free of disease progression (104 weeks maximum)

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: There is no statistical comparison for this single arm trial. The median of the posterior probability distribution for the true DCB rate was used to provide a Bayesian estimate of the DCB rate and 95% CrI. The anaysis conducted was a beta-binomial conjugate analysis using a Beta(1, 1) prior, this resulted in a bayesian estimate of DCB of 0.11 (95% CrI: 0.03, 0.22). 3 patients who reported durable clinical benefit, this resulted in a 0.002 probability that the true DCB rate was >= to 30%.

End point values	Nivolumab			
Subject group type	Reporting group			
Number of subjects analysed	35			
Units: Patients				
DCB	3			
Non-DCB	32			

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response

End point title	Objective Response

End point description:

Per Response Evaluation Criteria In Solid Tumors Criteria (RECIST v1.1) assessed by CT scan, objective response is the occurrence of Complete Response (CR) or Partial Response (PR) as the best overall response. Best overall response is the combined evaluation of target and non-target lesions, as provided in the protocol appendix 3.

Target lesions are evaluated as Complete Response (CR; disappearance of all target lesions), Partial Response (PR; >=30% decrease in the sum of the longest diameter), Progressive Disease (PD; >=20%

increase in the sum of the longest diameter) or Stable Disease (SD; insufficient shrinkage for PR or insufficient increase for PD).

Non-target lesions are evaluated as Complete Response (CR; disappearance of all non-target lesions), Incomplete Response/Stable Disease (SD; persistence of non-target lesions) or Progressive Disease (PD; new lesions and/or progression of existing non-target lesions).

End point type	Secondary

End point timeframe:

Trial treatment until disease progression (104 weeks maximum)

End point values	Nivolumab			
Subject group type	Reporting group			
Number of subjects analysed	35			
Units: Patients				
Objective Response Not Achieved	35			
Objective Response Achieved	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Best Percentage Change in Sum of Target Lesions

End point title	Best Percentage Change in Sum of Target Lesions

End point description:

At each evaluation, the longest diameters of all selected target lesions will be measured and summed and the percentage change from the baseline measurement will be calculated. The best percentage change is the one that reflects either the greatest decrease or the least increase over the whole period of assessment.

End point type	Secondary

End point timeframe:

Trial Treatment to disease progression (104 weeks maximum)

End point values	Nivolumab			
Subject group type	Reporting group			
Number of subjects analysed	30[2]			
Units: Percentage change				
arithmetic mean (standard deviation)	21.1 (± 18)			

Notes:

[2] - Only 30 had CT scans following baseline assessment, so this outcome could not be measured for 5 pts.

Statistical analyses

No statistical analyses for this end point

Secondary: Progression free survival time

End point title	Progression free survival time

End point description:

This is defined as the time from commencement of trial treatment to the date of CT scan when progressive disease first recorded or date of death without previously recorded progression.

End point type	Secondary

End point timeframe:

Time from commencement of trial treatment to the date of CT scan when progressive disease first recorded (104 weeks maximum)

End point values	Nivolumab			
Subject group type	Reporting group			
Number of subjects analysed	35			
Units: Weeks				
median (confidence interval 95%)	9 (8.7 to 9.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival Time

End point title	Overall Survival Time

End point description:

This is defined as the time from commencement of trial treatment to the date of death from any cause.

End point type	Secondary

End point timeframe:

Commencement of trial treatment until date of death; minimum of 18 months post-registration, if trial treatment was discontinued early, or up to 24 months post-registration for those completing trial treatment.

End point values	Nivolumab			
Subject group type	Reporting group			
Number of subjects analysed	35			
Units: Months				
median (confidence interval 95%)	7.2 (4.0 to 11.9)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the date of trial consent until 6 months after treatment discontinuation. If at the 6 month review time-point, any toxicities at grade 2 or higher related to trial treatment were still occurring, these were to be followed up until resolution.

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	4.03

Reporting groups

Reporting group title	Nivolumab

Reporting group description:

Nivolumab will be administered as a 60 minute IV infusion, with a window of -5 and +10 minutes, at a flat dose of 480mg. A dosing interval every 4 weeks (Q4W) was employed. Patients could receive nivolumab for a maximum of 2 years, or until disease progression, unacceptable toxicity or withdrawal of consent. With the first dose, cycle 1 day 1, to be given within 7 days of registration to the trial.

Serious adverse events	Nivolumab		
Total subjects affected by serious adverse events			
subjects affected / exposed	25 / 35 (71.43%)		
number of deaths (all causes)	29		
number of deaths resulting from adverse events	0		
Investigations			
Blood bilirubin increased			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Creatinine increased			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Depressed level of consciousness			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Seizure			

subjects affected / exposed	1 / 35 (2.86%)		
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 / 35 (2.86%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Fever			
subjects affected / exposed	4 / 35 (11.43%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 0		
Malaise			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Non-cardiac chest pain			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	6 / 35 (17.14%)		
occurrences causally related to treatment / all	1 / 6		
deaths causally related to treatment / all	0 / 0		
Ascites			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

Colonic obstruction				
subjects affected / exposed	2 / 35 (5.71%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Nausea				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Obstruction gastric				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Upper gastrointestinal hemorrhage				
subjects affected / exposed	2 / 35 (5.71%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	2 / 35 (5.71%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast disorders				
Vaginal discharge				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Dyspnea				
subjects affected / exposed	1 / 35 (2.86%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Confusion				

subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pelvic Pain			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Fever			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 0		
Infection			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infection secondary to Picc Line			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lung infection			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Peritoneal infection			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Upper respiratory infection			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hyperkalemia			
subjects affected / exposed	1 / 35 (2.86%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Nivolumab		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	35 / 35 (100.00%)		
Vascular disorders			
Thromboembolic Event			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	2		
General disorders and administration site conditions			
Chills			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	2		
Edema Limbs			
subjects affected / exposed	3 / 35 (8.57%)		
occurrences (all)	3		
Fatigue			
subjects affected / exposed	21 / 35 (60.00%)		
occurrences (all)	38		
Fever			

subjects affected / exposed occurrences (all) Malaise subjects affected / exposed occurrences (all) Non-Cardiac Chest Pain subjects affected / exposed occurrences (all) Pain subjects affected / exposed occurrences (all)	7 / 35 (20.00%) 9 2 / 35 (5.71%) 2 2 / 35 (5.71%) 4 2 / 35 (5.71%) 2		
Reproductive system and breast disorders Pelvic Pain subjects affected / exposed occurrences (all)	2 / 35 (5.71%) 6		
Respiratory, thoracic and mediastinal disorders Allergic Rhinitis subjects affected / exposed occurrences (all) Cough subjects affected / exposed occurrences (all) Dyspnea subjects affected / exposed occurrences (all) Productive Cough subjects affected / exposed occurrences (all)	2 / 35 (5.71%) 2 4 / 35 (11.43%) 4 9 / 35 (25.71%) 10 4 / 35 (11.43%) 7		
Psychiatric disorders Confusion subjects affected / exposed occurrences (all)	3 / 35 (8.57%) 3		
Investigations Alanine Aminotransferase Increased subjects affected / exposed occurrences (all)	5 / 35 (14.29%) 7		

Aspartate Aminotransferase Increased			
subjects affected / exposed	4 / 35 (11.43%)		
occurrences (all)	7		
LDH Increased			
subjects affected / exposed	3 / 35 (8.57%)		
occurrences (all)	3		
Raised Alkaline Phosphatase			
subjects affected / exposed	8 / 35 (22.86%)		
occurrences (all)	9		
Raised Bilirubin Levels			
subjects affected / exposed	5 / 35 (14.29%)		
occurrences (all)	14		
Raised C-Reactive Protein			
subjects affected / exposed	4 / 35 (11.43%)		
occurrences (all)	8		
Raised Creatinine			
subjects affected / exposed	4 / 35 (11.43%)		
occurrences (all)	6		
Weight Loss			
subjects affected / exposed	8 / 35 (22.86%)		
occurrences (all)	9		
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 35 (8.57%)		
occurrences (all)	4		
Peripheral Sensory Neuropathy			
subjects affected / exposed	3 / 35 (8.57%)		
occurrences (all)	3		
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	5 / 35 (14.29%)		
occurrences (all)	15		
Leukocytosis			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	2		
Gastrointestinal disorders			

Abdominal Distension				
subjects affected / exposed	3 / 35 (8.57%)			
occurrences (all)	3			
Abdominal Pain				
subjects affected / exposed	13 / 35 (37.14%)			
occurrences (all)	22			
Ascites				
subjects affected / exposed	3 / 35 (8.57%)			
occurrences (all)	4			
Colonic Obstruction				
subjects affected / exposed	2 / 35 (5.71%)			
occurrences (all)	2			
Constipation				
subjects affected / exposed	12 / 35 (34.29%)			
occurrences (all)	17			
Diarrhea				
subjects affected / exposed	11 / 35 (31.43%)			
occurrences (all)	18			
Dry Mouth				
subjects affected / exposed	5 / 35 (14.29%)			
occurrences (all)	6			
Mucositis Oral				
subjects affected / exposed	5 / 35 (14.29%)			
occurrences (all)	6			
Nausea				
subjects affected / exposed	14 / 35 (40.00%)			
occurrences (all)	31			
Small Intestinal Obstruction				
subjects affected / exposed	2 / 35 (5.71%)			
occurrences (all)	2			
Upper Gastrointestinal Hemorrhage				
subjects affected / exposed	2 / 35 (5.71%)			
occurrences (all)	2			
Vomiting				
subjects affected / exposed	10 / 35 (28.57%)			
occurrences (all)	18			

Skin and subcutaneous tissue disorders			
Dry Skin			
subjects affected / exposed	6 / 35 (17.14%)		
occurrences (all)	7		
Pruritus			
subjects affected / exposed	4 / 35 (11.43%)		
occurrences (all)	5		
Rash Acneiform			
subjects affected / exposed	3 / 35 (8.57%)		
occurrences (all)	3		
Rash Maculo-Papular			
subjects affected / exposed	3 / 35 (8.57%)		
occurrences (all)	4		
Renal and urinary disorders			
Acute Kidney Injury			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	3		
Urinary Frequency			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	2		
Urinary Tract Obstruction			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	2		
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	3 / 35 (8.57%)		
occurrences (all)	3		
Musculoskeletal and connective tissue disorders			
Back Pain			
subjects affected / exposed	10 / 35 (28.57%)		
occurrences (all)	14		
Flank Pain			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	2		
Infections and infestations			

Abdominal Infection			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	2		
Kidney Infection			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	2		
Lung Infection			
subjects affected / exposed	3 / 35 (8.57%)		
occurrences (all)	5		
Sepsis			
subjects affected / exposed	3 / 35 (8.57%)		
occurrences (all)	3		
Urinary Tract Infection			
subjects affected / exposed	8 / 35 (22.86%)		
occurrences (all)	9		
Wound Infection			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	2		
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	16 / 35 (45.71%)		
occurrences (all)	23		
Hyperglycemia			
subjects affected / exposed	2 / 35 (5.71%)		
occurrences (all)	2		
Hypoalbuminemia			
subjects affected / exposed	3 / 35 (8.57%)		
occurrences (all)	5		
Hyponatremia			
subjects affected / exposed	3 / 35 (8.57%)		
occurrences (all)	4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 April 2019	Substantial Amendment 1 (Protocol v3.0): Change to collect only month and year for date of birth. Clarification of follow-up period for pregnancies.
14 November 2019	Substantial Amendment 2 (Protocol v4.0): Addition of ISRCTN. Section 5.2: eRDC webpage amended. Addition of wording for new biopsy if archival biopsy is not sufficient or available. Change of PI at Beatson Cancer Centre.
20 May 2020	Substantial Amendment 3 (Protocol v5.0): Change in Class II expression requirements for eligibility. Addition of wording to allow treatment beyond progression if there is clinical benefit. Removal of fax number throughout. Clarification of pregnancy test requirements. Changes to assessment time points within the schedule of events to accommodate treatment dose changes. Change to treatment dose and schedule from 2 to 4 weekly. Addition of exploratory objective.
24 August 2021	Substantial Amendment 6 (Protocol v6.0): Changes to Table 3: Dose modification and toxicity management guidelines for immune-related AEs associated with nivolumab to include guidance from SPC (24-Aug-2020). Text added to schedule of assesments to clarify when an isotopic EGFR is needed. Text added to schedule of assesments to clarify the date that CT scans should be scheduled from. Schedule of Assessment tables updated to reflect that where applicable and acceptable in accordance to local practices, visits/assesments may be performed by telephone or video call. Process for remote consent added. Information relating to COVID-19 added.
01 November 2021	Substantial Amendment 8 (Protocol v7.0): Changes to Table 3 : Dose modification and toxicity management guidelines for immune-related AEs associated with nivolumab to include guidance from SPC.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/41407398