Clinical trial results:
A phase II trial of the addition of ipilumimab to carboplatin and etoposide chemotherapy for the first line treatment of extensive small cell lung cancer

Summary

EudraCT number	2010-021863-34
Trial protocol	GB
Global end of trial date	29 May 2014

Results information

Result version number	v1 (current)
This version publication date	29 December 2021
First version publication date	29 December 2021
Summary attachment (see zip file)	Trial Publication (1-s2.0-S1556086416305032-main.pdf)

Trial information

Trial identification

Sponsor protocol code	RHMCAN0739

Additional study identifiers

ISRCTN number	ISRCTN14095893
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Southampton University Hospitals NHS Trust
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Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	29 May 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 May 2014
Global end of trial reached?	Yes
Global end of trial date	29 May 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The trial aims to answer whether the addition of Ipilumimab to carboplatin and etoposide chemotherapy for patients with extensive stage small cell lung cancer is able to improve outcome for these patients as assessed by the proportion of patients alive and without progression at 1 year.

Protection of trial subjects:

1.3.4 Clinical safety with Ipilimumab
Ipilimumab immunotherapy is currently under investigation in patients with unresectable advanced melanoma (unresectable Stage III or Stage IV) to potentially demonstrate an improvement on a large unmet medical need in this population.
Ipilimumab has been administered to approximately 2901 patients with different cancers in 25 completed or ongoing clinical trials as of 31-Mar-2009 with a dose range between 0.3 mg/kg and 20 mg/kg and in various combinations.
In general, the safety profile of Ipilimumab administered as single doses of up to 20 mg/kg and multiple doses of up to 10 mg/kg every 3 weeks was characterized by adverse reactions that were mostly immune in nature. Drug-related SAEs were reported in studies of Ipilimumab administered as monotherapy, as well as in combination with vaccines, cytokines, Chemotherapy, or radiation therapy.
The overall summary of safety for the 2901 patients treated with Ipilimumab in the completed or ongoing clinical trials and the subset of 658 patients treated at the 10 mg/kg dose level is presented in Table 1.

Table 1: Ipilimumab - Overall Summary of Safety

	Number of Patients (%) Ipilimumab 0.3 - 20 mg/kg N = 2901	Ipilimumab 10 mg/kg N = 658
Any Drug-related AE	2357 (81.2)	561 (85.3)
Grade 1	699 (24.1)	158 (24.0)
Grade 2	889 (30.6)	198 (30.1)
Grade 3	617 (21.3)	163 (24.8)
Grade 4	127 (4.4)	38 (5.8)
Grade 5	20 (0.7)	4 (0.6)
Any Serious Adverse Events	1258 (43.4)	310 (47.1)
Grade 3 - 4	806 (27.8)	179 (27.2)
Any Drug-related Serious Adverse Events	595 (20.5)	179 (27.2)
Grade 3 - 4	469 (16.2)	140 (21.3)

Complete information on the clinical safety with Ipilimumab can be found in the current Ipilimumab Investigator Brochure (IB).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 June 2011
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: 42
Worldwide total number of subjects	42
EEA total number of subjects	42

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)	32
From 65 to 84 years	10
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 42 patients were enrolled between September 2011 and April 2014; 39 were evaluable for safety and 38 for efficacy

Pre-assignment

Screening details:

The patients were men and women aged 18 and older who had a histological or cytological diagnosis of SCLC; no previous systemic therapy for SCLC; an Eastern Cooperative Oncology Group performance status of 0 or 1; adequate baseline laboratory test results; and no active or chronic infection with human immunodeficiency virus, hepatitis B, or hepatit

Period 1

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

Arms

Arm title	Combination therapy
Arm description: -	
Arm type	Single
Investigational medicinal product name	IPILUMUMAB
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion in administration system
Routes of administration	Intravenous drip use

Dosage and administration details:

10mg/kg

Number of subjects in period 1	Combination therapy
Started	42
1 year pf survival data collected	39
Completed	39
Not completed	3
Patient choice, patient choice	2
Protocol deviation	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description:

Forty-two patients with no previous systemic therapy for SCLC were registered into this study between September 2011 and April 2014 at six sites in the United Kingdom

Reporting group values	Overall trial	Total	
Number of subjects	42	42	
Age categorical Units: Subjects			
Age continuous Units: years median full range (min-max)	 63 44 to 84	 -	
Gender categorical Units: Subjects			
Female Male	15 27	15 27	

End points

End points reporting groups

Reporting group title	Combination therapy

Reporting group description: -

Primary: 1-year PFS according to RECIST v 1.0

End point title	1-year PFS according to RECIST v 1.0[1]

End point description:

95% Confidence Interval estimated using Wilson Interval

End point type	Primary

End point timeframe:

The primary end point was 1-year PFS according to RECIST v 1.0. PFS was defined as the time from day 1 of the first cycle of chemotherapy to the date of progression or death from any cause.

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: Single arm trial

End point values	Combination therapy			
Subject group type	Reporting group			
Number of subjects analysed	38			
Units: percentage				
number (confidence interval 95%)	15.8 (7.4 to 30.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: irPFS at 1 year

End point title	irPFS at 1 year

End point description:

End point type	Secondary

End point timeframe:

1 year

End point values	Combination therapy			
Subject group type	Reporting group			
Number of subjects analysed	38			
Units: percentage				
number (confidence interval 95%)	12.6 (4.0 to 26.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Median Overall Survival

End point title	Median Overall Survival

End point description:

End point type	Secondary

End point timeframe:

Duration of Trial

End point values	Combination therapy			
Subject group type	Reporting group			
Number of subjects analysed	38			
Units: Months				
median (confidence interval 95%)	17.0 (7.9 to 24.3)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Timeframe for AE

Adverse event reporting additional description:

AE additional description

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	Combination therapy

Reporting group description: -

Serious adverse events	Combination therapy		
Total subjects affected by serious adverse events			
subjects affected / exposed	36 / 42 (85.71%)		
number of deaths (all causes)	8		
number of deaths resulting from adverse events	8		
Vascular disorders			
Thromboembolic event	Additional description: Thromboembolic event		
subjects affected / exposed	3 / 42 (7.14%)		
occurrences causally related to treatment / all	2 / 3		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Fatigue	Additional description: Fatigue		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Fever	Additional description: Fever		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Autoimmune disorder	Additional description: Autoimmune disorder		

subjects affected / exposed	2 / 42 (4.76%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Aspiration	Additional description: Aspiration		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Bronchopulmonary hemorrhage	Additional description: Bronchopulmonary hemorrhage		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pulmonary fibrosis	Additional description: Pulmonary fibrosis		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Dyspnoea	Additional description: Dyspnoea		
subjects affected / exposed	3 / 42 (7.14%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 1		
Investigations			
Alanine aminotransferase increased	Additional description: Alanine aminotransferase increased		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Blood antidiuretic hormone abnormal	Additional description: Blood antidiuretic hormone abnormal		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Other - Transamintis	Additional description: Other - Transamintis		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Neutrophil count decreased	Additional description: Neutrophil count decreased		
subjects affected / exposed	3 / 42 (7.14%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiac arrest	Additional description: Cardiac arrest		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Atrial fibrillation	Additional description: Atrial fibrillation		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Other - Bells palsy	Additional description: Other - Bells palsy		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Headache	Additional description: Headache		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences causally related to treatment / all	2 / 3		
deaths causally related to treatment / all	0 / 0		
Seizure	Additional description: Seizure		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Other - Immune related central neuropathy	Additional description: Other - Immune related central neuropathy		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Dizziness	Additional description: Dizziness		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Blood and lymphatic system disorders			
Febrile neutropenia	Additional description: Febrile neutropenia		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Pancytopenia	Additional description: Pancytopenia		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia	Additional description: Thrombocytopenia		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Anaemia	Additional description: Anaemia		
subjects affected / exposed	4 / 42 (9.52%)		
occurrences causally related to treatment / all	2 / 4		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Colitis	Additional description: Colitis		
subjects affected / exposed	4 / 42 (9.52%)		
occurrences causally related to treatment / all	5 / 5		
deaths causally related to treatment / all	0 / 0		
Constipation	Additional description: Constipation		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diarrhoea	Additional description: Diarrhoea		
subjects affected / exposed	12 / 42 (28.57%)		
occurrences causally related to treatment / all	14 / 15		
deaths causally related to treatment / all	0 / 0		
Gastric haemorrhage	Additional description: Gastric haemorrhage		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	1 / 1		

Nausea	Additional description: Nausea		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Other - Ileitis	Additional description: Other - Ileitis		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Rash maculo-papular	Additional description: Rash maculo-papular		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Generalised muscle weakness (Neurological)	Additional description: Generalised muscle weakness (Neurological)		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Other - Bilateral leg weakness	Additional description: Other - Bilateral leg weakness		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pain	Additional description: Pain		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Generalised muscle weakness (Other)	Additional description: Generalised muscle weakness (Other)		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Chest infection	Additional description: Chest infection		

subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lower Respiratory Tract Infection	Additional description: Lower Respiratory Tract Infection		
subjects affected / exposed	3 / 42 (7.14%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Sepsis	Additional description: Sepsis		
subjects affected / exposed	3 / 42 (7.14%)		
occurrences causally related to treatment / all	2 / 3		
deaths causally related to treatment / all	1 / 1		
Other - Clostridium difficile	Additional description: Other - Clostridium difficile		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lung infection	Additional description: Lung infection		
subjects affected / exposed	5 / 42 (11.90%)		
occurrences causally related to treatment / all	2 / 5		
deaths causally related to treatment / all	2 / 2		
Infection	Additional description: Infection		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Upper respiratory infection	Additional description: Upper respiratory infection		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hypomagnesaemia	Additional description: Hypomagnesaemia		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hyperglycaemia	Additional description: Hyperglycaemia		

subjects affected / exposed	2 / 42 (4.76%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Combination therapy		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	42 / 42 (100.00%)		
Vascular disorders			
Hypotension	Additional description: Hypotension		
subjects affected / exposed	4 / 42 (9.52%)		
occurrences (all)	4		
Hot flashes	Additional description: Hot flashes		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Thromboembolic event	Additional description: Thromboembolic event		
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Superficial thrombophlebitis	Additional description: Superficial thrombophlebitis		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
General disorders and administration site conditions			
Flu like symptoms	Additional description: Flu like symptoms		
subjects affected / exposed	7 / 42 (16.67%)		
occurrences (all)	7		
Fatigue	Additional description: Fatigue		
subjects affected / exposed	33 / 42 (78.57%)		
occurrences (all)	52		
Night sweats	Additional description: Night sweats		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Oedema limbs	Additional description: Oedema limbs		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Chills	Additional description: Chills		

subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Fever	Additional description: Fever		
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Pain	Additional description: Pain		
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Neck oedema	Additional description: Neck oedema		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	2		
Non-cardiac chest pain	Additional description: Non-cardiac chest pain		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Localised oedema	Additional description: Localised oedema		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Immune system disorders			
Autoimmune disorder	Additional description: Autoimmune disorder		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Allergic reaction	Additional description: Allergic reaction		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Mucositis	Additional description: Mucositis		
subjects affected / exposed	7 / 42 (16.67%)		
occurrences (all)	9		
Bronchspasm	Additional description: Bronchspasm		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Sore throat	Additional description: Sore throat		
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Dyspnoea	Additional description: Dyspnoea		

subjects affected / exposed	16 / 42 (38.10%)		
occurrences (all)	33		
Cough	Additional description: Cough		
subjects affected / exposed	10 / 42 (23.81%)		
occurrences (all)	12		
Lung infection	Additional description: Lung infection		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Upper respiratory infection	Additional description: Upper respiratory infection		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Pulmonary fibrosis	Additional description: Pulmonary fibrosis		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Aspiration	Additional description: Aspiration		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Hoarseness	Additional description: Hoarseness		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Productive cough	Additional description: Productive cough		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Bronchopulmonary hemorrhage	Additional description: Bronchopulmonary hemorrhage		
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	4		
Psychiatric disorders			
Other - Increased anxiety/agitation	Additional description: Other - Increased anxiety/agitation		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Agitation	Additional description: Agitation		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Depression	Additional description: Depression		
subjects affected / exposed	5 / 42 (11.90%)		
occurrences (all)	7		

Insomnia	Additional description: Insomnia		
subjects affected / exposed	12 / 42 (28.57%)		
occurrences (all)	13		
Confusion	Additional description: Confusion		
subjects affected / exposed	4 / 42 (9.52%)		
occurrences (all)	7		
Anxiety	Additional description: Anxiety		
subjects affected / exposed	4 / 42 (9.52%)		
occurrences (all)	5		
Investigations			
Neutrophil count decreased	Additional description: Neutrophil count decreased		
subjects affected / exposed	14 / 42 (33.33%)		
occurrences (all)	25		
Activated partial thromboplastin time prolonged	Additional description: Activated partial thromboplastin time prolonged		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Blood bilirubin increased	Additional description: Blood bilirubin increased		
subjects affected / exposed	5 / 42 (11.90%)		
occurrences (all)	6		
Aspartate aminotransferase increased	Additional description: Aspartate aminotransferase increased		
subjects affected / exposed	4 / 42 (9.52%)		
occurrences (all)	8		
Alanine aminotransferase increased	Additional description: Alanine aminotransferase increased		
subjects affected / exposed	7 / 42 (16.67%)		
occurrences (all)	9		
Lymphocyte count decreased	Additional description: Lymphocyte count decreased		
subjects affected / exposed	10 / 42 (23.81%)		
occurrences (all)	22		
Lymphocyte count increased	Additional description: Lymphocyte count increased		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
INR increased	Additional description: INR increased		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Alkaline phosphatase increased	Additional description: Alkaline phosphatase increased		

subjects affected / exposed	10 / 42 (23.81%)		
occurrences (all)	24		
Lymphopenia	Additional description: Lymphopenia		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Other - Transamintis	Additional description: Other - Transamintis		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Elevated lactate dehydrogenase	Additional description: Elevated lactate dehydrogenase		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Platelet count decreased	Additional description: Platelet count decreased		
subjects affected / exposed	7 / 42 (16.67%)		
occurrences (all)	8		
White blood cell decreased	Additional description: White blood cell decreased		
subjects affected / exposed	6 / 42 (14.29%)		
occurrences (all)	11		
Blood antidiuretic hormone abnormal	Additional description: Blood antidiuretic hormone abnormal		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Creatinine increased	Additional description: Creatinine increased		
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	5		
GGT increased	Additional description: GGT increased		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	3		
Weight loss	Additional description: Weight loss		
subjects affected / exposed	6 / 42 (14.29%)		
occurrences (all)	7		
Cardiac disorders			
Cardiac arrest	Additional description: Cardiac arrest		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Chest pain - cardiac	Additional description: Chest pain - cardiac		
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		

Atrial fibrillation	Additional description: Atrial fibrillation		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Nervous system disorders			
Cognitive disturbance	Additional description: Cognitive disturbance		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Peripheral neuropathy	Additional description: Peripheral neuropathy		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Light headed	Additional description: Light headed		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Seizure	Additional description: Seizure		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Other - Neuropathy	Additional description: Other - Neuropathy		
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Concentration impairment	Additional description: Concentration impairment		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Dizziness	Additional description: Dizziness		
subjects affected / exposed	8 / 42 (19.05%)		
occurrences (all)	10		
Dysarthria	Additional description: Dysarthria		
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Paraesthesia	Additional description: Paraesthesia		
subjects affected / exposed	4 / 42 (9.52%)		
occurrences (all)	5		
Memory impairment	Additional description: Memory impairment		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Facial nerve disorder	Additional description: Facial nerve disorder		

subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Dysgeusia	Additional description: Dysgeusia		
subjects affected / exposed	4 / 42 (9.52%)		
occurrences (all)	6		
Lethargy	Additional description: Lethargy		
subjects affected / exposed	4 / 42 (9.52%)		
occurrences (all)	4		
Tremour	Additional description: Tremour		
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Somnolence	Additional description: Somnolence		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	2		
Peripheral sensory neuropathy	Additional description: Peripheral sensory neuropathy		
subjects affected / exposed	4 / 42 (9.52%)		
occurrences (all)	4		
Amnesia	Additional description: Amnesia		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Facial muscle weakness	Additional description: Facial muscle weakness		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	3		
Other - Nervous system disorder	Additional description: Other - Nervous system disorder		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Headache	Additional description: Headache		
subjects affected / exposed	13 / 42 (30.95%)		
occurrences (all)	18		
Movements involuntary	Additional description: Movements involuntary		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	3		
Other - Focal seizures	Additional description: Other - Focal seizures		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Blood and lymphatic system disorders			

Other - Raised platelets	Additional description: Other - Raised platelets		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Febrile neutropenia	Additional description: Febrile neutropenia		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Anaemia	Additional description: Anaemia		
subjects affected / exposed	21 / 42 (50.00%)		
occurrences (all)	58		
Thrombocytopenia	Additional description: Thrombocytopenia		
subjects affected / exposed	5 / 42 (11.90%)		
occurrences (all)	9		
Pancytopenia	Additional description: Pancytopenia		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Ear and labyrinth disorders			
Ear pain	Additional description: Ear pain		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Hearing impaired	Additional description: Hearing impaired		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Other - Inner ear popping sensation	Additional description: Other - Inner ear popping sensation		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Eye disorders			
Other - Right subconjunctival haemorrhage	Additional description: Other - Right subconjunctival haemorrhage		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Eye pain	Additional description: Eye pain		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Watering eyes	Additional description: Watering eyes		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Gastrointestinal disorders			

Oesophageal pain	Additional description: Oesophageal pain		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Diarrhoea	Additional description: Diarrhoea		
subjects affected / exposed	28 / 42 (66.67%)		
occurrences (all)	60		
Mucositis oral	Additional description: Mucositis oral		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Nausea	Additional description: Nausea		
subjects affected / exposed	24 / 42 (57.14%)		
occurrences (all)	39		
Other - Soreness & dermal adema to buccal mucose and vulva	Additional description: Other - Soreness & dermal adema to buccal mucose and vulva		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Vomiting	Additional description: Vomiting		
subjects affected / exposed	17 / 42 (40.48%)		
occurrences (all)	19		
Other - Ileitis	Additional description: Other - Ileitis		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Rectal hemorrhage	Additional description: Rectal hemorrhage		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	2		
Stomach pain	Additional description: Stomach pain		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Flatulence	Additional description: Flatulence		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Dysgeusia	Additional description: Dysgeusia		
subjects affected / exposed	5 / 42 (11.90%)		
occurrences (all)	5		
Dysphagia	Additional description: Dysphagia		

subjects affected / exposed	4 / 42 (9.52%)		
occurrences (all)	5		
Dyspepsia	Additional description: Dyspepsia		
subjects affected / exposed	9 / 42 (21.43%)		
occurrences (all)	10		
Abdominal pain	Additional description: Abdominal pain		
subjects affected / exposed	11 / 42 (26.19%)		
occurrences (all)	18		
Constipation	Additional description: Constipation		
subjects affected / exposed	16 / 42 (38.10%)		
occurrences (all)	18		
Gastric haemorrhage	Additional description: Gastric haemorrhage		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Anorexia	Additional description: Anorexia		
subjects affected / exposed	7 / 42 (16.67%)		
occurrences (all)	10		
Pain	Additional description: Pain		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Haemorrhoids	Additional description: Haemorrhoids		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Sore mouth	Additional description: Sore mouth		
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Colitis	Additional description: Colitis		
subjects affected / exposed	5 / 42 (11.90%)		
occurrences (all)	6		
Dry mouth	Additional description: Dry mouth		
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	4		
Dental caries	Additional description: Dental caries		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Bloating	Additional description: Bloating		

subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Mucositis	Additional description: Mucositis		
subjects affected / exposed	6 / 42 (14.29%)		
occurrences (all)	7		
Skin and subcutaneous tissue disorders			
Other - Facial rash + upper shoulder rash	Additional description: Other - Facial rash + upper shoulder rash		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Other - Facial rash	Additional description: Other - Facial rash		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Pruritus	Additional description: Pruritus		
subjects affected / exposed	11 / 42 (26.19%)		
occurrences (all)	15		
Dry skin	Additional description: Dry skin		
subjects affected / exposed	4 / 42 (9.52%)		
occurrences (all)	6		
Urticaria	Additional description: Urticaria		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Other - Facial redness puffiness	Additional description: Other - Facial redness puffiness		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Scalp pain	Additional description: Scalp pain		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Other - Facial swelling	Additional description: Other - Facial swelling		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Alopecia	Additional description: Alopecia		
subjects affected / exposed	20 / 42 (47.62%)		
occurrences (all)	23		
Palmar-plantar erythrodysesthesia syndrome	Additional description: Palmar-plantar erythrodysesthesia syndrome		

subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Rash	Additional description: Rash		
subjects affected / exposed	21 / 42 (50.00%)		
occurrences (all)	31		
Rash maculo-papular	Additional description: Rash maculo-papular		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Renal and urinary disorders			
Urinary retention	Additional description: Urinary retention		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Dysuria	Additional description: Dysuria		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Endocrine disorders			
Hypothyroidism	Additional description: Hypothyroidism		
subjects affected / exposed	5 / 42 (11.90%)		
occurrences (all)	7		
Hyperthyroidism	Additional description: Hyperthyroidism		
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Other - thyroiditis	Additional description: Other - thyroiditis		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	2		
Cushingoid	Additional description: Cushingoid		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Neck pain	Additional description: Neck pain		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Generalised muscle weakness (Other)	Additional description: Generalised muscle weakness (Other)		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Arthralgia	Additional description: Arthralgia		

subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Myalgia	Additional description: Myalgia		
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Other - Ache in right arm	Additional description: Other - Ache in right arm		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Generalised muscle weakness (Neurological)	Additional description: Generalised muscle weakness (Neurological)		
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Pain	Additional description: Pain		
subjects affected / exposed	15 / 42 (35.71%)		
occurrences (all)	20		
Bone pain	Additional description: Bone pain		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Back pain	Additional description: Back pain		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Other - Bilateral leg weakness	Additional description: Other - Bilateral leg weakness		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Infections and infestations			
Upper respiratory infection	Additional description: Upper respiratory infection		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	3		
Eye infection	Additional description: Eye infection		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Sepsis	Additional description: Sepsis		
subjects affected / exposed	4 / 42 (9.52%)		
occurrences (all)	4		
Oral thrush	Additional description: Oral thrush		

subjects affected / exposed	6 / 42 (14.29%)		
occurrences (all)	6		
Infection	Additional description: Infection		
subjects affected / exposed	6 / 42 (14.29%)		
occurrences (all)	6		
Skin infection	Additional description: Skin infection		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Upper respiratory tract infection	Additional description: Upper respiratory tract infection		
subjects affected / exposed	4 / 42 (9.52%)		
occurrences (all)	4		
Lip infection	Additional description: Lip infection		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Other - Viral infection	Additional description: Other - Viral infection		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Urinary tract infection	Additional description: Urinary tract infection		
subjects affected / exposed	6 / 42 (14.29%)		
occurrences (all)	6		
Ear infection	Additional description: Ear infection		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Other - Clostridium difficile	Additional description: Other - Clostridium difficile		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Anorectal infection	Additional description: Anorectal infection		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Lung infection	Additional description: Lung infection		
subjects affected / exposed	6 / 42 (14.29%)		
occurrences (all)	6		
Lower Respiratory Tract Infection	Additional description: Lower Respiratory Tract Infection		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Chest infection	Additional description: Chest infection		

subjects affected / exposed	5 / 42 (11.90%)		
occurrences (all)	5		
Metabolism and nutrition disorders			
Hypercalcaemia	Additional description: Hypercalcaemia		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	2		
Anorexia	Additional description: Anorexia		
subjects affected / exposed	11 / 42 (26.19%)		
occurrences (all)	14		
Hypermagnesemia	Additional description: Hypermagnesemia		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Hypoalbuminaemia	Additional description: Hypoalbuminaemia		
subjects affected / exposed	10 / 42 (23.81%)		
occurrences (all)	32		
Hypocalcaemia	Additional description: Hypocalcaemia		
subjects affected / exposed	5 / 42 (11.90%)		
occurrences (all)	6		
Dehydration	Additional description: Dehydration		
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Hypomagnesaemia	Additional description: Hypomagnesaemia		
subjects affected / exposed	10 / 42 (23.81%)		
occurrences (all)	24		
Hyperglycaemia	Additional description: Hyperglycaemia		
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Hypokalaemia	Additional description: Hypokalaemia		
subjects affected / exposed	9 / 42 (21.43%)		
occurrences (all)	17		
Hyponatraemia	Additional description: Hyponatraemia		
subjects affected / exposed	8 / 42 (19.05%)		
occurrences (all)	27		
Hypophosphataemia	Additional description: Hypophosphataemia		
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported