Clinical trial results:
A phase II trial of pembrolizumab in patients with non-small cell lung cancer and a performance status of 2

Summary

EudraCT number	2015-002241-55
Trial protocol	GB
Global end of trial date	07 February 2023

Results information

Result version number	v1 (current)
This version publication date	23 October 2026
First version publication date	23 October 2026

Trial information

Trial identification

Sponsor protocol code	RG_14-172

Additional study identifiers

ISRCTN number	ISRCTN10047797
ClinicalTrials.gov id (NCT number)	NCT02733159
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University of Birmingham
Sponsor organisation address	Edgbaston, Birmingham, United Kingdom, B15 2TT
Public contact	PePS2 Clinical Trial Coordinator, University of Birmingham, PePS2@trials.bham.ac.uk
Scientific contact	Professor Gary Middleton, University of Birmingham, PePS2@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	31 January 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 November 2022
Global end of trial reached?	Yes
Global end of trial date	07 February 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The first primary objective of this trial is to determine that pembrolizumab is safe and tolerable at the selected dose of 200 mg 3 weekly in non-small cell lung cancer patients with a physician scored ECOG Performance Status of 2.
The second primary objective is to allow detection of durable clinical benefit to justify further investigator subsequent studies.

Protection of trial subjects:

All adverse events and serious adverse events experienced by participants in the clinical trial were collected by the trial team.

A Trial Steering Committee (TSC) was involved to protect and serve PePS2 trial patients (especially in relation to safety) and to assist and advise the Chief Investigator and other members of the Trial Management Group (TMG) so as to protect the validity and credibility of the trial. This was to safeguard the interests of participants, assess the safety and efficacy of the interventions, and monitor the overall conduct of the clinical trial. A risk assessment was also in place to document any potential risks of the trial and how these would be minimised.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 November 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 62
Worldwide total number of subjects	62
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)	15
From 65 to 84 years	46
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

The PePS2 trial opened to recruitment on 07-Nov-2016, with the first patient being recruited on 04-Jan-2017. The last patient was recruited on 13-Feb-2018 when the trial was closed to recruitment. The total number of patients recruited was 62.

Pre-assignment

Screening details:

PD-L1 expression was measured from either an archived biopsy or a newly obtained biopsy. Confirmation of PD-L1 status was required prior to patient being registered. A full screening evaluation was also performed to ensure that the patient satisfied all of the eligibility criteria.

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	Arm 1

Arm description:

Pembrolizumab, every 3 weeks, 200 mg, IV infusion

Arm type	Experimental
Investigational medicinal product name	Pembrolizumab
Investigational medicinal product code	MK3475
Other name	KEYTRUDA
Pharmaceutical forms	Concentrate for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

200 mg, 3 weekly, administered as a 30 minute IV infusion

Number of subjects in period 1	Arm 1
Started	62
Completed	7
Not completed	55
Consent withdrawn by subject	5
Adverse event, non-fatal	8
Death	8
Not specified	6
Did not start trial treatment	2
Lack of efficacy	26

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	62	62	
Age categorical Units: Subjects			
Adults (18-64 years)	15	15	
From 65-84 years	46	46	
85 years and over	1	1	
Age continuous Units: years			
arithmetic mean	69.85		
standard deviation	± 8.01	-	
Gender categorical Units: Subjects			
Female	28	28	
Male	34	34	
Histology Units: Subjects			
Adenocarcinoma	43	43	
Adenosquamous Carcinoma	0	0	
Squamous Cell Carcinoma	12	12	
Not Otherwise Specified	1	1	
Other	6	6	
Smoking Status Units: Subjects			
Current smoker	11	11	
Ex-smoker	45	45	
Never smoked	3	3	
Not Known	3	3	
Sample Type			
Only given for patients who had a successful PD-L1 staining of the tumour sample. Denominator is therefore N=59 for these items			
Units: Subjects			
Archived biopsy sample	52	52	
New biopsy sample	7	7	
Not applicable	3	3	
PD-L1 staining result			
Only given for patients who had a successful PD-L1 staining of the tumour sample. Denominator is therefore N=59 for these items.			
Units: Subjects			
Negative (<1%)	28	28	
Positive (1-49%)	16	16	
Strong Positive (50-100%)	15	15	
Not applicable	3	3	

Line of therapy Units: Subjects			
First	25	25	
Subsequent	37	37	
Pack Years Units: Years			
arithmetic mean	43.78		
standard deviation	± 26.6	-	
Duration of abstinence Units: Years			
arithmetic mean	15.38		
standard deviation	± 16.13	-	
Charlson Co-Morbidity Index Score Units: Score			
arithmetic mean	7.58		
standard deviation	± 3.04	-	
Tumour Cells Expressing PD-L1 Units: percent			
arithmetic mean	24.89		
standard deviation	± 36.19	-	

End points

End points reporting groups

Reporting group title	Arm 1
Reporting group description:	
Pembrolizumab, every 3 weeks, 200 mg, IV infusion	

Primary: Durable Clinical Benefit Rate

End point title	Durable Clinical Benefit Rate[1]
End point description:	
Patients will have CT scans every 9 weeks from baseline until disease progression. On each occasion, overall tumour burden will be assessed using RECIST version 1.1. The efficacy co-primary outcome measure for the trial is durable clinical benefit defined as the occurrence of CR, PR or SD without prior progressive disease at or after the second scheduled CT scan (scheduled to occur at 18 weeks).	
End point type	Primary
End point timeframe:	
≥18 weeks, up to maximum of 2 years	
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: This is a single-arm trial, so there are no comparison groups for statistical analysis. An event rate of 37% was observed (95% CI: 26%, 49%).	

End point values	Arm 1			
Subject group type	Reporting group			
Number of subjects analysed	60			
Units: Patients				
Patients Experiencing DCB Event	22			
Patients Not Experiencing DCB Event	38			

Statistical analyses

No statistical analyses for this end point

Primary: Toxicity Rate

End point title	Toxicity Rate[2]
End point description:	
Adverse events will be recorded in relation to each cycle of treatment and graded according to CTCAE criteria. The toxicity co-primary outcome measure for the trial is defined as the occurrence of a treatment-related dose delay or treatment discontinuation due to toxicity.	
End point type	Primary
End point timeframe:	
Date of patient registration until 6 months after the administration of the last treatment (a maximum of 2 years treatment and 6 months followup after end of treatment)	
Notes:	
[2] - 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: This is a single-arm trial, so there are no comparison groups for statistical analysis. An event rate of 30% was observed (95% CI: 20%, 43%).	

End point values	Arm 1			
Subject group type	Reporting group			
Number of subjects analysed	60			
Units: Patients				
Patients Experiencing Toxicity Event	18			
Patients Not Experiencing Toxicity	42			

Statistical analyses

No statistical analyses for this end point

Secondary: Objective response (OR)

End point title	Objective response (OR)

End point description:

Objective response (OR) is the occurrence of Complete Response (CR) or Partial Response (PR) as the best overall response. OR will be based on responses confirmed using the subsequent 9-weekly scan but OR based on unconfirmed responses will also be reported.
The estimated median (90% Confidence Interval) for follow up time is 14.6 months (90% CI: 12.1, NA months). Note the upper estimate of the confidence interval was not attained, meaning the endpoint could not be entered onto the system.

End point type	Secondary

End point timeframe:

≥18 weeks, up to maximum of 2 years

End point values	Arm 1			
Subject group type	Reporting group			
Number of subjects analysed	60			
Units: Patients				
No	44			
Yes	16			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to progression

End point title	Time to progression

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. Patients with no recorded progression at the time of analysis or who die without recorded progression will be censored at the date of the CT scan when they were last recorded with an evaluable measure that was not progression.

End point type	Secondary

End point timeframe:

Time to progression up to 2 years

End point values	Arm 1			
Subject group type	Reporting group			
Number of subjects analysed	60			
Units: Months				
median (confidence interval 90%)	11.9 (4.13 to 27.8)			

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. Patients who are alive with no recorded progression at the time of analysis will be censored at the date of the CT scan when they were last recorded with an evaluable measure that was not progression.

End point type	Secondary

End point timeframe:

Progression-free survival time up to 2 years

End point values	Arm 1			
Subject group type	Reporting group			
Number of subjects analysed	60			
Units: Months				
median (confidence interval 90%)	4.39 (3.48 to 9.9)			

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. Patients who are alive at the time of analysis will be censored at the date last seen alive.

End point type	Secondary

End point timeframe:

Survival time up to 2 years or date of death

End point values	Arm 1			
Subject group type	Reporting group			
Number of subjects analysed	60			
Units: month				
median (confidence interval 90%)	9.8 (6.77 to 13)			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Stable Disease

End point title	Duration of Stable Disease

End point description:

This is defined as the time from commencement of trial treatment to the date of the subsequent CT scan when progressive disease is first confirmed or date of death without previously recorded progression. This outcome is calculated and reported separately for patients who achieve an Objective Response (OR) or Stable Disease (SD). Patients experiencing OR or SD who are alive with no recorded progression at the time of analysis will be censored at the date of the CT scan when they were last recorded with an evaluable measure that was not progression.

End point type	Secondary

End point timeframe:

Survival time up to 2 years or date of death

End point values	Arm 1			
Subject group type	Reporting group			
Number of subjects analysed	60			
Units: month				
median (confidence interval 90%)	4.39 (3.97 to 6.77)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Details of all treatment-related AEs will be documented and reported from the date of registration until 6 months after the administration of the last treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	4.03

Reporting groups

Reporting group title	Arm 1

Reporting group description:

Pembrolizumab, every 3 weeks, 200 mg, IV infusion

Serious adverse events	Arm 1		
Total subjects affected by serious adverse events			
subjects affected / exposed	51 / 60 (85.00%)		
number of deaths (all causes)	48		
number of deaths resulting from adverse events	19		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Other - Malignant neoplasm			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Other - Death			
subjects affected / exposed	5 / 60 (8.33%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 4		
Vascular disorders			
Hypotension			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Superior vena cava syndrome			

subjects affected / exposed	1 / 60 (1.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Fever				
subjects affected / exposed	3 / 60 (5.00%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Other - Unknown	Additional description: Death was reportable as an SAE, however, some of the SAEs were submitted retrospectively in error and the cause of death was unknown.			
subjects affected / exposed	7 / 60 (11.67%)			
occurrences causally related to treatment / all	0 / 7			
deaths causally related to treatment / all	0 / 7			
Respiratory, thoracic and mediastinal disorders				
Laryngeal hemorrhage				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory failure				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Other - Haemoptysis				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Other - Lung infection				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Other - Respiratory distress				

subjects affected / exposed	1 / 60 (1.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Hypoxia				
subjects affected / exposed	2 / 60 (3.33%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Pleural effusion				
subjects affected / exposed	2 / 60 (3.33%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	1 / 1			
Pneumonitis				
subjects affected / exposed	2 / 60 (3.33%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Other - Shortness of Breath				
subjects affected / exposed	2 / 60 (3.33%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Other - Death				
subjects affected / exposed	7 / 60 (11.67%)			
occurrences causally related to treatment / all	0 / 7			
deaths causally related to treatment / all	0 / 7			
Dyspnea				
subjects affected / exposed	10 / 60 (16.67%)			
occurrences causally related to treatment / all	0 / 15			
deaths causally related to treatment / all	0 / 2			
Psychiatric disorders				
Confusion				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Investigations				

Alanine aminotransferase increased			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac arrest			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Other - Death			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Nervous system disorders			
Ataxia			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dizziness			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dysphasia			

subjects affected / exposed	1 / 60 (1.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Other - Nervous system				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Seizure				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Stroke				
subjects affected / exposed	2 / 60 (3.33%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 1			
Ear and labyrinth disorders				
Vestibular disorder				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Other - Acute Kidney Injury				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Mucositis oral				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				

subjects affected / exposed	4 / 60 (6.67%)		
occurrences causally related to treatment / all	3 / 4		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Other - Hepatobiliary disorders			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Flank pain			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Back pain			
subjects affected / exposed	3 / 60 (5.00%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 1		
Infections and infestations			
Other - Chest Infection			

subjects affected / exposed	1 / 60 (1.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Other - Infection				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Other - Pneumonia				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Other - Shortness of Breath				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Urinary tract infection				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Lung infection				
subjects affected / exposed	3 / 60 (5.00%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Hypercalcemia				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Hypokalemia				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Anorexia				

subjects affected / exposed	3 / 60 (5.00%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 3		

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

Non-serious adverse events	Arm 1		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	58 / 60 (96.67%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Other - Death			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Superior vena cava syndrome			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	2		
Vasculitis			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Hypotension			
subjects affected / exposed	3 / 60 (5.00%)		
occurrences (all)	3		
Thromboembolic event			
subjects affected / exposed	3 / 60 (5.00%)		
occurrences (all)	4		
General disorders and administration site conditions			
Chills			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Flu like symptoms			

subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Abdominal pain				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Chest wall discomfort (occasional)				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Cough				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Dehydration				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Edema feet				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Hair thinning				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Head cold				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Itch				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Leg Cramps				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Poor appetitie				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Raised sputum viscosity				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			

Other - Sore throat subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1		
Other - Swollen feet and ankles subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1		
Other - Weight loss subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1		
Infusion related reaction subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1		
Non-cardiac chest pain subjects affected / exposed occurrences (all)	3 / 60 (5.00%) 3		
Malaise subjects affected / exposed occurrences (all)	5 / 60 (8.33%) 6		
Edema limbs subjects affected / exposed occurrences (all)	7 / 60 (11.67%) 8		
Fever subjects affected / exposed occurrences (all)	9 / 60 (15.00%) 11		
Pain subjects affected / exposed occurrences (all)	9 / 60 (15.00%) 10		
Fatigue subjects affected / exposed occurrences (all)	36 / 60 (60.00%) 62		
Immune system disorders Other - Rash subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1		
Respiratory, thoracic and mediastinal disorders			

Bronchopulmonary hemorrhage				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Hoarseness				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	2			
Laryngeal hemorrhage				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Pleuritic pain				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Pneumonitis				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Pulmonary edema				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Bronchitis				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Cap-community acquired pneumonia				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Chest pain				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Exacerbation of copd				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Increased sputum-brown				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Lower respiratory track infection				

subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Lower respiratory tract infection				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Lung crackles				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Mucositis				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Reduced air entry and a few creps				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Reduced air entry to right lung				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Reduced air entry to the right lower lobe				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Reduced breath sounds left upper lobe				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Respiratory distress				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Respiratory infection				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Right basal chest infection				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Scattered creps				

subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Shortness of breath				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Shortness of breath on minimal exertion				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - White phlegm				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Sore throat				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	2			
Other - Chest infection				
subjects affected / exposed	2 / 60 (3.33%)			
occurrences (all)	2			
Productive cough				
subjects affected / exposed	3 / 60 (5.00%)			
occurrences (all)	5			
Other - Exacerbation of chronic obstructive pulmonary disease				
subjects affected / exposed	3 / 60 (5.00%)			
occurrences (all)	3			
Other - Pneumonia				
subjects affected / exposed	3 / 60 (5.00%)			
occurrences (all)	3			
Pleural effusion				
subjects affected / exposed	4 / 60 (6.67%)			
occurrences (all)	4			
Other - Haemoptysis				
subjects affected / exposed	4 / 60 (6.67%)			
occurrences (all)	4			
Hypoxia				

subjects affected / exposed	5 / 60 (8.33%)		
occurrences (all)	5		
Cough			
subjects affected / exposed	21 / 60 (35.00%)		
occurrences (all)	31		
Dyspnea			
subjects affected / exposed	29 / 60 (48.33%)		
occurrences (all)	48		
Psychiatric disorders			
Confusion			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		
Depression			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		
Insomnia			
subjects affected / exposed	4 / 60 (6.67%)		
occurrences (all)	4		
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Blood bilirubin increased			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	2		
Blood corticotrophin decreased			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
GGT increased			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Other - Cortisol low			

subjects affected / exposed occurrences (all) Other - Hyperbilirubinemia subjects affected / exposed occurrences (all) Other - Ldh raised - 794 (uln 480) subjects affected / exposed occurrences (all) Other - Thyroid stimulating hormone increased subjects affected / exposed occurrences (all) Lymphocyte count decreased subjects affected / exposed occurrences (all) Serum amylase increased subjects affected / exposed occurrences (all) Alanine aminotransferase increased subjects affected / exposed occurrences (all) Creatinine increased subjects affected / exposed occurrences (all) Weight loss subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1 1 / 60 (1.67%) 1 1 / 60 (1.67%) 1 1 / 60 (1.67%) 1 1 / 60 (1.67%) 1 1 / 60 (1.67%) 1 2 / 60 (3.33%) 2 3 / 60 (5.00%) 4 3 / 60 (5.00%) 3		
Injury, poisoning and procedural complications Bruising subjects affected / exposed occurrences (all) Fall subjects affected / exposed occurrences (all)	 1 / 60 (1.67%) 1 3 / 60 (5.00%) 3		
Cardiac disorders			

Cardiac arrest			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Other - Ejection systolic murmor			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Heart failure			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Myocardial infarction			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Palpitations			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Sinus bradycardia			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Atrial fibrillation			
subjects affected / exposed	3 / 60 (5.00%)		
occurrences (all)	3		
Nervous system disorders			
Ataxia			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Concentration impairment			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Dysphasia			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Memory impairment			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Other - Involuntary neck movements			

subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Pins & needles in right arm during antibiotic infusion				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Tingling in extremeties				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Nystagmus				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Seizure				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Stroke				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Tremor				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Lethargy				
subjects affected / exposed	2 / 60 (3.33%)			
occurrences (all)	2			
Paresthesia				
subjects affected / exposed	2 / 60 (3.33%)			
occurrences (all)	2			
Peripheral sensory neuropathy				
subjects affected / exposed	2 / 60 (3.33%)			
occurrences (all)	2			
Headache				
subjects affected / exposed	5 / 60 (8.33%)			
occurrences (all)	6			
Dizziness				
subjects affected / exposed	6 / 60 (10.00%)			
occurrences (all)	9			

Blood and lymphatic system disorders			
Other - Creatinine decreased			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Other - Haemoptysis			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Other - Hypercalcemia			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Thrombocytopenia			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Anemia			
subjects affected / exposed	5 / 60 (8.33%)		
occurrences (all)	8		
Ear and labyrinth disorders			
Other - Hearing reduction			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Vestibular disorder			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Eye disorders			
Other - Age related reduced visual acuity			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Other - Thromboembolic event left eye			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Watering eyes			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Gastrointestinal disorders			
Colitis			

subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Dry mouth				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Altered taste				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Decreased appetite				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Gastric reflux				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Reflux				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Mucositis oral				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	3			
Dyspepsia				
subjects affected / exposed	2 / 60 (3.33%)			
occurrences (all)	5			
Dysphagia				
subjects affected / exposed	2 / 60 (3.33%)			
occurrences (all)	2			
Abdominal pain				
subjects affected / exposed	3 / 60 (5.00%)			
occurrences (all)	3			
Diarrhoea				
subjects affected / exposed	14 / 60 (23.33%)			
occurrences (all)	21			
Vomiting				
subjects affected / exposed	14 / 60 (23.33%)			
occurrences (all)	20			
Constipation				

subjects affected / exposed	15 / 60 (25.00%)		
occurrences (all)	24		
Nausea			
subjects affected / exposed	15 / 60 (25.00%)		
occurrences (all)	21		
Hepatobiliary disorders			
Other - Bilirubin increased			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Other - Drug induced liver injury			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Other - Raised alk phosphate			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Other - Abdominal rash			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Other - Blisters on hands			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Other - Dry skin			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Other - Dry skin on legs			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Other - Dry skin under right eye			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	2		
Other - Fungal skin rash			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Other - Infected sebaceous cycst			

subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Itch				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Itch skin				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Itching				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Itchy face				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Itchy skin				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Papulopustular				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Pitting oedema				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Pressure ulcer				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Psoriasis rash				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Rash on legs				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Rash on the legs and arms				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Red legs and mild oedema				

subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Skin lesion to scalp				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Sore feet and toes				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Sore naval				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Ulcer on left foot				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - X2 sore spots to upper right chest				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Skin ulceration				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Rash acneiform				
subjects affected / exposed	2 / 60 (3.33%)			
occurrences (all)	5			
Other - Skin rash				
subjects affected / exposed	2 / 60 (3.33%)			
occurrences (all)	3			
Pruritus				
subjects affected / exposed	3 / 60 (5.00%)			
occurrences (all)	5			
Other - Rash				
subjects affected / exposed	3 / 60 (5.00%)			
occurrences (all)	5			
Dry skin				
subjects affected / exposed	6 / 60 (10.00%)			
occurrences (all)	7			

Rash maculo-papular subjects affected / exposed occurrences (all)	12 / 60 (20.00%) 14		
Renal and urinary disorders Cystitis noninfective subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1		
Proteinuria subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 3		
Other - Raised creatinine subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1		
Other - Renal failure subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1		
Other - Urinary infection subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1		
Other - Worsening of renal function subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1		
Urinary frequency subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1		
Chronic kidney disease subjects affected / exposed occurrences (all)	3 / 60 (5.00%) 3		
Acute kidney injury subjects affected / exposed occurrences (all)	4 / 60 (6.67%) 6		
Endocrine disorders Other - Adrenal insufficiency subjects affected / exposed occurrences (all)	1 / 60 (1.67%) 1		
Other - Hypophysitis			

subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Adrenal insufficiency				
subjects affected / exposed	2 / 60 (3.33%)			
occurrences (all)	2			
Hyperthyroidism				
subjects affected / exposed	2 / 60 (3.33%)			
occurrences (all)	3			
Hypothyroidism				
subjects affected / exposed	8 / 60 (13.33%)			
occurrences (all)	9			
Musculoskeletal and connective tissue disorders				
Muscle weakness left-sided				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Muscle weakness lower limb				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Muscle weakness upper limb				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Bruising to left arm (garden gate hit it)				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Discitis				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Generalised muscle weakness				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	2			
Other - Generalized muscle weakness				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Heavy and painful left calf				

subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Joint pain				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Left arm pain				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Left hip/ pelvic pain				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Left sided gluteal pain				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Leg ache				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Muscle pain				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Muscle spasms				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	2			
Other - Right hand weakness				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Osteoporosis				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Pain in extremity				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Arthralgia				
subjects affected / exposed	2 / 60 (3.33%)			
occurrences (all)	3			
Flank pain				

subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	4		
Other - Knee pain			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		
Other - Left shoulder pain			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		
Myalgia			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	3		
Neck pain			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		
Back pain			
subjects affected / exposed	14 / 60 (23.33%)		
occurrences (all)	25		
Infections and infestations			
Bronchial infection			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Other - Chest infections			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Other - Chest sepsis			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Other - Cystitis			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Other - Genital candida			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Other - Infected picc line			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		

Other - Lower respiratory track infection				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	2			
Other - Lower respiratory tract infection				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Oral candida				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Oral candidiasis				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Picc line infection				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Presumed uti				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Thrush				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Undefined infection				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Unwell				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Viral infection				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Other - Viral infection around mouth				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences (all)	1			
Papulopustular rash				

subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Other - Oral thrush			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		
Skin infection			
subjects affected / exposed	3 / 60 (5.00%)		
occurrences (all)	3		
Other - Chest infection			
subjects affected / exposed	6 / 60 (10.00%)		
occurrences (all)	11		
Upper respiratory infection			
subjects affected / exposed	6 / 60 (10.00%)		
occurrences (all)	7		
Lung infection			
subjects affected / exposed	10 / 60 (16.67%)		
occurrences (all)	12		
Urinary tract infection			
subjects affected / exposed	10 / 60 (16.67%)		
occurrences (all)	16		
Metabolism and nutrition disorders			
Hypercalcemia			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	2		
Hypoalbuminemia			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Hypocalcemia			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Other - Low b12			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Obesity			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		

Dehydration			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		
Hyperglycemia			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		
Hypokalemia			
subjects affected / exposed	3 / 60 (5.00%)		
occurrences (all)	3		
Hypomagnesemia			
subjects affected / exposed	6 / 60 (10.00%)		
occurrences (all)	9		
Hyponatremia			
subjects affected / exposed	6 / 60 (10.00%)		
occurrences (all)	12		
Anorexia			
subjects affected / exposed	20 / 60 (33.33%)		
occurrences (all)	28		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 March 2016	Substantial Amendment 01: Update to protocol (v2.0) and patient documents
20 July 2016	Substantial Amendment 02: Addition of new sites
30 January 2017	Substantial Amendment 03: Update to protocol (v3.0) and patient documents
04 May 2017	Substantial Amendment 04: Update to Reference Safety Information (v2.0)
14 June 2017	Substantial Amendment 05: Update to protocol (v4.0) and patient documents
14 August 2017	Substantial Amendment 06: Update to protocol (v5.0)
10 July 2018	Substantial Amendment 07: Update to protocol (v6.0)
16 January 2019	Substantial Amendment 08: Update to Reference Safety Information (v4.0)
24 June 2019	Substantial Amendment 09: Addition of a second QP site in the CTA application
21 January 2020	Substantial Amendment 10: Update to Reference Safety Information (v5.0)
12 January 2021	Substantial Amendment 11: Change of PI

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/32199466