Clinical trial results:
A Pilot Study of Combined Immune Checkpoint Inhibition in combination with ablative therapies in Subjects with Hepatocellular Carcinoma (HCC).

Summary

EudraCT number	2019-002767-98
Trial protocol	IE
Global end of trial date	12 December 2022

Results information

Result version number	v1 (current)
This version publication date	31 August 2025
First version publication date	31 August 2025

Trial information

Trial identification

Sponsor protocol code	UCDCRC/19/01

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	University College Dublin
Sponsor organisation address	Catherine McAuley Centre, Nelson Street, Dublin 7, Ireland, D07 A8NN
Public contact	Gráinne O'Reilly, Director of Research Clinical Trials, University College Dublin, +353 17166603, grainne.oreilly1@ucd.ie
Scientific contact	Gráinne O'Reilly, Director of Research Clinical Trials, University College Dublin, +353 17166603, grainne.oreilly1@ucd.ie

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	07 September 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 December 2022
Global end of trial reached?	Yes
Global end of trial date	12 December 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To preliminarily evaluate the 6-month progression free survival (PFS) of combining tremelimumab and durvalumab in patients with advanced HCC (in combination with TACE). The trial protocol is derived from a US-based trial (with ClinicalTrials.gov id number 16-C-0135) sponsored by the NIH. A combined analysis will be undertaken but results from the Irish cohort only are reported here.

Protection of trial subjects:

The clinical research team (chief investigator, clinical trial nurse, research registrar, co- investigators) will meet on a regular (at least monthly) basis during the accrual and active treatment phase of the study to review eligibility of prospective participants and review safety data of patients and discuss each patient already enrolled. Decisions about dose level enrollment and dose escalation if applicable will be made based on the toxicity data from prior patients.

All data will be collected in a timely manner and reviewed by the principal investigator or a lead associate investigator. Adverse events will be reported as required above. Any safety concerns, new information that might affect either the ethical and or scientific conduct of the trial, or protocol deviations will be immediately reported to the IRB, the Sponsor and the manufacturer.

The principal investigator will review adverse event and response data on each patient to ensure safety and data accuracy. The principal investigator will personally conduct or supervise the investigation and provide appropriate delegation of responsibilities to other members of the research staff.

Background therapy:

N/A

Evidence for comparator:

N/A

Actual start date of recruitment	31 October 2019
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	Ireland: 13
Worldwide total number of subjects	13
EEA total number of subjects	13

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)	0
From 65 to 84 years	13
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment of patients onto this study was through standard Centre for Cancer Research (CCR) mechanisms. The study will be posted on the CCR website and on clinicaltrials.gov. For all patients participating in Ireland their cases were discussed at the GI Multidisciplinary meeting for review of imaging and adjudication of eligibility.

Pre-assignment

Screening details:

Before registration, each potential patient was given a PIL and written informed consent was obtained according to the requirements of ICH GCP. Only patients fulfilling all inclusion criteria (as checked by the investigator or designee), and without any exclusion criteria were entered for registration.

Period 1

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

Blinding implementation details:

This is a single arm, open-label study.

Arms

Are arms mutually exclusive?	Yes
Arm title	Main cohort

Arm description:

The 10 subjects enrolled in the main trial cohort were treated as follows:
TACE as per SOC +
Tremelimumab 300mg for 1 dose +
Durvalumab 1500mg flat dose q28 days until end of study treatment

Arm type	Experimental
Investigational medicinal product name	Tremelimumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Tremelimumab 300mg for 1 dose. Tremelimumab is to be administered as an IV solution of 10 mg/kg at a rate of 250 mL/hr, followed by observation for 60 minutes.

Investigational medicinal product name	Durvalumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Dose of 1500mg durvalumab for patients >30 kg will be administered using an IV bag containing 0.9% (w/v) saline, with a final durvalumab concentration ranging from 1 to 20mg/mL, and delivered through an IV administration set with a 0.2- or 0.22-µm in-line filter. Dose of 1500mg durvalumab for patients >30 kg will be administered using an IV bag containing 0.9% (w/v) saline, with a final durvalumab concentration ranging from 1 to 20mg/mL, and delivered through an IV administration set with a 0.2- or 0.22-µm in-line filter.

Arm title	Pilot

Arm description:

The first three subjects enrolled in this trial were treated with the below previously tested dosing

schedule as a ‘lead in’ to improve the overall conduct of the study and minimize risk. A previous study in the US tested the below dosing schedule and demonstrated feasibility and safety.

TACE as per SOC
Tremelimumab 75mg for 4 doses q28 days
Durvalumab 1500mg flat dose q28 days until end of study treatment

Arm type	Pilot study
Investigational medicinal product name	Tremelimumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Infusion

Dosage and administration details:

Tremelimumab 75mg for 4 doses q28 days. Tremelimumab is administered as an IV solution of 10 mg/kg at a rate of 250 mL/hr, followed by observation for 60 minutes.

Investigational medicinal product name	Durvalumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Infusion

Dosage and administration details:

Dose of 1500mg durvalumab for patients >30 kg will be administered using an IV bag containing 0.9% (w/v) saline, with a final durvalumab concentration ranging from 1 to 20mg/mL, and delivered through an IV administration set with a 0.2- or 0.22-µm in-line filter. Dose of 1500mg durvalumab for patients >30 kg will be administered using an IV bag containing 0.9% (w/v) saline, with a final durvalumab concentration ranging from 1 to 20mg/mL, and delivered through an IV administration set with a 0.2- or 0.22-µm in-line filter.

Number of subjects in period 1	Main cohort	Pilot
Started	10	3
Completed	10	3

Baseline characteristics

Reporting groups	
Reporting group title	Main cohort

Reporting group description:

The 10 subjects enrolled in the main trial cohort were treated as follows:
TACE as per SOC +
Tremelimumab 300mg for 1 dose +
Durvalumab 1500mg flat dose q28 days until end of study treatment

Reporting group title	Pilot

Reporting group description:

The first three subjects enrolled in this trial were treated with the below previously tested dosing schedule as a 'lead in' to improve the overall conduct of the study and minimize risk. A previous study in the US tested the below dosing schedule and demonstrated feasibility and safety.

TACE as per SOC
Tremelimumab 75mg for 4 doses q28 days
Durvalumab 1500mg flat dose q28 days until end of study treatment

Reporting group values	Main cohort	Pilot	Total
Number of subjects	10	3	13
Age categorical Units: Subjects			
<=18 years	0	0	0
Between 18 and 65 years	2	0	2
>65 years	8	3	11
Age continuous Units: years			
median	69.5	71.0	
inter-quartile range (Q1-Q3)	67.2 to 72.0	71.0 to 71.0	-
Gender categorical Units: Subjects			
Female	1	1	2
Male	9	2	11
Ethnicity Units: Subjects			
White	10	3	13
Black or Black Irish	0	0	0
Asian or Asian Irish	0	0	0
Other (including mixed background)	0	0	0
Prior surgery Units: Subjects			
Yes	2	2	4
No	8	1	9
Prior TACE Units: Subjects			
Yes	5	1	6
No	5	2	7
Prior Ablation Units: Subjects			

Yes	1	1	2
No	9	2	11
Prior Chemotherapy Units: Subjects			
Yes	2	0	2
No	8	3	11
ECOG Performance Status Units: Subjects			
status 0	7	2	9
status 1	3	1	4
status 2	0	0	0
status 3	0	0	0
status 4	0	0	0
status 5	0	0	0
Hepatitis B Units: Subjects			
Positive - Acute	0	0	0
Positive - Chronic	0	0	0
Negative - Not Immune	8	1	9
Negative - Immune	2	1	3
Indeterminate	0	0	0
N-Miss	0	1	1
Hepatitis C Units: Subjects			
Positive - Current Infection	2	0	2
Negative - Past Infection	0	0	0
Negative	8	3	11
Indeterminate	0	0	0
TB Testing Units: Subjects			
Positive	0	0	0
Negative	0	0	0
Testing Not Clinically Indicated	10	3	13
HIV status Units: Subjects			
Positive	0	0	0
Negative	10	3	13
Indeterminate	0	0	0
Months from diagnosis to first study treatment visit Units: Months			
median	3	27.8	
inter-quartile range (Q1-Q3)	2.3 to 22.1	15 to 36.7	-

End points

End points reporting groups

Reporting group title	Main cohort

Reporting group description:

The 10 subjects enrolled in the main trial cohort were treated as follows:
TACE as per SOC +
Tremelimumab 300mg for 1 dose +
Durvalumab 1500mg flat dose q28 days until end of study treatment

Reporting group title	Pilot

Reporting group description:

The first three subjects enrolled in this trial were treated with the below previously tested dosing schedule as a 'lead in' to improve the overall conduct of the study and minimize risk. A previous study in the US tested the below dosing schedule and demonstrated feasibility and safety.

TACE as per SOC
Tremelimumab 75mg for 4 doses q28 days
Durvalumab 1500mg flat dose q28 days until end of study treatment

Primary: Six month progression free survival (PFS)

End point title	Six month progression free survival (PFS)

End point description:

The primary endpoint is defined as survival without progression (evaluated by RECIST) to 6 months, with follow-up starting from the day of trial treatment initiation.

End point type	Primary

End point timeframe:

From treatment initiation to 6-months

End point values	Main cohort	Pilot		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	3		
Units: Subjects				
Yes	6	1		
No	4	2		

Statistical analyses

Statistical analysis title	Primary endpoint analysis

Statistical analysis description:

The primary efficacy endpoint of 6-month PFS is estimated along with a 90% one-sided lower confidence bound, calculated using the 'survival' package in R with confidence interval estimated based on the logarithmic transformation of the survival function. Analysis was performed on the main trial cohort of 10 patients. A 90% one-sided lower confidence bound above 0.15 (15%) was defined in the protocol as providing evidence of a clinically relevant treatment effect.

Comparison groups	Main cohort v Pilot

Number of subjects included in analysis	13
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.0014
Method	Kaplan-Meier progression free survival
Parameter estimate	Proportion
Point estimate	0.6
Confidence interval	
level	90 %
sides	1-sided
lower limit	0.431

Notes:

[1] - The exact binomial test is performed to investigate whether or not the sample data provide evidence that the 6-months progression-free survival in subjects treated with this intervention is greater than 15%, testing at a significance level of 10%

Secondary: Median progression free survival (PFS) time

End point title	Median progression free survival (PFS) time

End point description:

Estimate of median progression free survival (PFS) time, as defined by RECIST, using data collected from treatment initiation to end of follow-up. Note that confidence interval upper bounds were not estimable- a value of 999 has been entered in place to comply with EudraCT validation rules.

End point type	Secondary

End point timeframe:

From treatment initiation until end of follow-up

End point values	Main cohort	Pilot		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	3		
Units: Months				
median (confidence interval 90%)	6.4 (3.6 to 999)	3.7 (3.4 to 999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Best overall response rate

End point title	Best overall response rate

End point description:

RECIST Best Overall Response rates

End point type	Secondary

End point timeframe:

From treatment initiation to end of follow-up

End point values	Main cohort	Pilot		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	3		
Units: Subjects				
Complete response	0	0		
Partial response	0	0		
Stable disease	7	3		
Progressive disease	3	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival time

End point title	Overall survival time

End point description:

This endpoint is used to estimate median overall survival time, from survival data captured from treatment initiation until last survival follow-up. Note that confidence interval upper bounds were not estimable - a value of 999 has been entered in place to comply with EudraCT validation rules.

End point type	Secondary

End point timeframe:

From treatment initiation until last survival follow-up

End point values	Main cohort	Pilot		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	3		
Units: Months				
median (confidence interval 90%)	21.1 (9.4 to 999)	14.7 (3.4 to 999)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The adverse event reporting period for this trial began from the time of informed consent up to 90 days after the last dose of study drug has been administered.

Adverse event reporting additional description:

Given the potential risk for delayed immune-related toxicities, safety follow-up was performed up to 90 days after the last dose of Durvalumab or Tremelimumab administration. The extended safety follow-up beyond 30 days (to 90 days) after last durvalumab or tremelimumab administration was performed either via a site visit or via a telephone call.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26

Reporting groups

Reporting group title	Main cohort

Reporting group description:

The final 10 subjects enrolled in the trial were treated as follows:
TACE as per SOC +
Tremelimumab 300mg for 1 dose +
Durvalumab 1500mg flat dose q28 days until end of study treatment

Reporting group title	Pilot

Reporting group description:

The first three subjects enrolled in this trial were treated with the below previously tested dosing schedule as a 'lead in' to improve the overall conduct of the study and minimize risk. A previous study in the US tested the below dosing schedule and demonstrated feasibility and safety.
TACE as per SOC
Tremelimumab 75mg for 4 doses q28 days
Durvalumab 1500mg flat dose q28 days until end of study treatment

Serious adverse events	Main cohort	Pilot	
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 10 (70.00%)	1 / 3 (33.33%)	
number of deaths (all causes)	7	3	
number of deaths resulting from adverse events	2	1	
Investigations			
Blood bilirubin increased	Additional description: 10005364 Blood bilirubin increased		
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatine increased	Additional description: 10005464 Blood creatine increased		
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Transaminases increased	Additional description: 10054889 Transaminases increased		
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Hospitalisation	Additional description: 10054112 Hospitalisation		
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Hepatic encephalopathy	Additional description: 10019660 Hepatic encephalopathy		
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lethargy	Additional description: 10024264 Lethargy		
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia	Additional description: 10003549 Asthenia		
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise	Additional description: 10025482 Malaise		
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disease progression	Additional description: 10061818 Disease progression		
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gastrointestinal disorders			
Abdominal pain lower	Additional description: 10000084 Abdominal pain lower		

subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea	Additional description: 10012735 Diarrhoea		
subjects affected / exposed	2 / 10 (20.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea	Additional description: 10028813 Nausea		
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Liver disorder	Additional description: 10024670 Liver disorder		
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism	Additional description: 10037377 Pulmonary embolism		
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia	Additional description: 10003239 Arthralgia		
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscular weakness	Additional description: 10028372 Muscular weakness		
subjects affected / exposed	0 / 10 (0.00%)	1 / 3 (33.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Neck pain	Additional description: 10028836 Neck pain		

subjects affected / exposed	2 / 10 (20.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Infection	Additional description: 10021789 Infection		
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyperkalaemia	Additional description: 10020646 Hyperkalaemia		
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Decreased appetite	Additional description: 10061428 Decreased appetite		
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Main cohort	Pilot	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 10 (90.00%)	3 / 3 (100.00%)	
General disorders and administration site conditions			
Oedema	Additional description: 10030095 Oedema		
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Peripheral swelling	Additional description: 10048959 Peripheral swelling		
subjects affected / exposed	1 / 10 (10.00%)	1 / 3 (33.33%)	
occurrences (all)	1	1	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea	Additional description: 10013968 Dyspnoea		
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Pneumonitis	Additional description: 10035742 Pneumonitis		

subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Investigations			
Blood glucose increased	Additional description: 10005557 Blood glucose increased		
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Blood magnesium decreased	Additional description: 10005654 Blood magnesium decreased		
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Blood thyroid stimulating hormone increased	Additional description: 10005833 Blood thyroid stimulating hormone increased		
subjects affected / exposed	0 / 10 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
C-reactive protein increased	Additional description: 10006825 C-reactive protein increased		
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Haemoglobin decreased	Additional description: 10018884 Haemoglobin decreased		
subjects affected / exposed	2 / 10 (20.00%)	0 / 3 (0.00%)	
occurrences (all)	2	0	
Thyroid function test abnormal	Additional description: 10043730 Thyroid function test abnormal		
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Thyroxine increased	Additional description: 10043818 Thyroxine increased		
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Platelet count increased	Additional description: 10051608 Platelet count increased		
subjects affected / exposed	0 / 10 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Fall	Additional description: 10016173 Fall		
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Dizziness	Additional description: 10013573 Dizziness		
subjects affected / exposed	0 / 10 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Headache	Additional description: 10019211 Headache		

subjects affected / exposed	2 / 10 (20.00%)	0 / 3 (0.00%)	
occurrences (all)	2	0	
Lethargy	Additional description: 10024264 Lethargy		
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	
occurrences (all)	2	0	
Memory impairment	Additional description: 10027175 Memory impairment		
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Anaemia	Additional description: 10002034 Anaemia		
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Abdominal distension	Additional description: 10000060 Abdominal distension		
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Abdominal pain	Additional description: 10000081 Abdominal pain		
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Defaecation urgency	Additional description: 10012110 Defaecation urgency		
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Diarrhoea	Additional description: 10012735 Diarrhoea		
subjects affected / exposed	2 / 10 (20.00%)	0 / 3 (0.00%)	
occurrences (all)	2	0	
Dry mouth	Additional description: 10013781 Dry mouth		
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Nausea	Additional description: 10028813 Nausea		
subjects affected / exposed	3 / 10 (30.00%)	1 / 3 (33.33%)	
occurrences (all)	3	1	
Hepatobiliary disorders			
Jaundice	Additional description: 10023126 Jaundice		
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			

Alopecia	Additional description: 10001760 Alopecia		
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Dermatitis	Additional description: 10012431 Dermatitis		
subjects affected / exposed	2 / 10 (20.00%)	0 / 3 (0.00%)	
occurrences (all)	3	0	
Pruritus	Additional description: 10037087 Pruritus		
subjects affected / exposed	3 / 10 (30.00%)	1 / 3 (33.33%)	
occurrences (all)	4	1	
Rash	Additional description: 10037844 Rash		
subjects affected / exposed	2 / 10 (20.00%)	0 / 3 (0.00%)	
occurrences (all)	2	0	
Rash pruritic	Additional description: 10037884 Rash pruritic		
subjects affected / exposed	0 / 10 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Haematuria	Additional description: 10018867 Haematuria		
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Endocrine disorders			
Hyperthyroidism	Additional description: 10020850 Hyperthyroidism		
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Hypothyroidism	Additional description: 10021114 Hypothyroidism		
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Arthropathy	Additional description: 10003285 Arthropathy		
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Back pain	Additional description: 10003988 Back pain		
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Pain in extremity	Additional description: 10033425 Pain in extremity		
subjects affected / exposed	0 / 10 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	

Twitching of limbs	Additional description: 10045203 Twitching of limbs		
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Herpes zoster	Additional description: 10019974 Herpes zoster		
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Urinary tract infection	Additional description: 10046571 Urinary tract infection		
subjects affected / exposed	0 / 10 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
COVID-19	Additional description: 10084268 COVID-19		
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Dehydration	Additional description: 10012174 Dehydration		
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Fluid retention	Additional description: 10016807 Fluid retention		
subjects affected / exposed	2 / 10 (20.00%)	0 / 3 (0.00%)	
occurrences (all)	2	0	
Hypokalaemia	Additional description: 10021015 Hypokalaemia		
subjects affected / exposed	1 / 10 (10.00%)	0 / 3 (0.00%)	
occurrences (all)	2	0	

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