Clinical trial results:
A multi-centre randomised study of induction chemotherapy followed by capecitabine (+/-nelfinavir) with high or standard dose radiotherapy for locally advanced non-metastatic pancreatic cancer

Summary

EudraCT number	2013-004968-56
Trial protocol	GB
Global end of trial date	07 July 2021

Results information

Result version number	v1 (current)
This version publication date	28 October 2023
First version publication date	28 October 2023

Trial information

Trial identification

Sponsor protocol code	OCTO_063

Additional study identifiers

ISRCTN number	ISRCTN50083238
ClinicalTrials.gov id (NCT number)	NCT02024009
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University of Oxford
Sponsor organisation address	1st floor, Boundary Brook House Churchill Drive, Headington, Oxford, United Kingdom, OX3 7GB
Public contact	SCALOP-2 Clinical Trial Coordinator, Oncology Clinical Trials Office, 0044 1865617078, octo-scalop-2@oncology.ox.ac.uk
Scientific contact	SCALOP-2 Clinical Trial Coordinator, Oncology Clinical Trials Office, 0044 1865617078, octo-scalop-2@oncology.ox.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	27 September 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 July 2021
Global end of trial reached?	Yes
Global end of trial date	07 July 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The objective of Stage 1 was to determine the Maximum Tolerated Dose (MTD) of nelfinavir to be administered alongside chemoradiotherapy and therefore to establish the dose of nelfinavir to be taken forward into Stage 2.

There are 2 co-principal research objectives of Stage 2 which are:

1. Does increasing radiotherapy dose schedule from 50.4Gy (in 28 fractions) to 60Gy (in 30 fractions) improve the overall survival (OS) in LAPC?
2. Does the addition of nelfinavir to chemoradiotherapy improve progression free survival (PFS) in locally advanced non-metastatic pancreatic cancer?

The aim is to select the best chemoradiotherapy regimen/s that can be taken forward to compare against chemotherapy alone in order to define the best treatment for this group of patients.

Protection of trial subjects:

The protocol was conducted in compliance with the UK Clinical Trials Regulations, the Principles of Good Clinical Practice (GCP) and the applicable policies of the sponsoring organisation. Together, these implement the ethical principles of the Declaration of Helsinki (1996) and the regulatory requirementsfor clinical trials of investigational medicinal products under the European Union Clinical Trials Directive.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 May 2016
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: 159
Worldwide total number of subjects	159
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	61
From 65 to 84 years	98
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The first patient recruited was on 18Aug2017 and the last patient recruited was on 10Mar2020. The expected end of recruitment was May 2020 but due to the COVID-19 pandemic and remaining trial timelines, a decision was made to close recruitment early.

Pre-assignment

Screening details:

At least 559 participants were assessed for eligibility and consent, 400 (71.6%) were excluded from recruitment, of whom 377 were either ineligible or declined consent or eligible but did not proceed to be registered or not consented for other reasons.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A

Arm description:

Capecitabine (830mg/m2 oral bd) + nelfinavir + 50.4Gy in 28#

Arm type	Experimental
Investigational medicinal product name	Capecitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

capecitabine (830mg/m2 oral bd) for 28 days

Arm title	Arm B

Arm description:

Capecitabine (830mg/m2 oral bd) + 50.4Gy in 28#

Arm type	Experimental
Investigational medicinal product name	Capecitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

capecitabine (830mg/m2 oral bd) for 28 days

Arm title	Arm C

Arm description:

Capecitabine (830mg/m2 oral bd) + nelfinavir** + 60Gy in 30#

Arm type	Experimental

Investigational medicinal product name	Capecitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:
capecitabine (830mg/m2 oral bd) for 30 days

Arm title	Arm D

Arm description:
Capecitabine (830mg/m2 oral bd) + 60Gy in 30#

Arm type	Experimental
Investigational medicinal product name	Capecitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:
capecitabine (830mg/m2 oral bd) for 30 days

Number of subjects in period 1[1]	Arm A	Arm B	Arm C
Started	19	26	19
Completed	15	23	16
Not completed	4	3	3
Patient decision	1	2	-
Physician decision	1	-	-
Disease progression	1	1	2
Patient able to move to surgery	1	-	-
Patient suitable for surgery	-	-	1

Number of subjects in period 1[1]	Arm D
Started	27
Completed	23
Not completed	4
Patient decision	2
Physician decision	-
Disease progression	2
Patient able to move to surgery	-
Patient suitable for surgery	-

Notes:
[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: The trial recruited 159 subjects and the results focus on the 91 subjects who had the

therapy being studied by the trial.

Baseline characteristics

Reporting groups	
Reporting group title	Arm A
Reporting group description:	
Capecitabine (830mg/m2 oral bd) + nelfinavir + 50.4Gy in 28#	

Reporting group title	Arm B
Reporting group description:	
Capecitabine (830mg/m2 oral bd) + 50.4Gy in 28#	

Reporting group title	Arm C
Reporting group description:	
Capecitabine (830mg/m2 oral bd) + nelfinavir** + 60Gy in 30#	

Reporting group title	Arm D
Reporting group description:	
Capecitabine (830mg/m2 oral bd) + 60Gy in 30#	

Reporting group values	Arm A	Arm B	Arm C
Number of subjects	19	26	19
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	7	14	8
From 65-84 years	12	12	11
85 years and over	0	0	0
Age continuous Units: years			
median	70	62.5	69
inter-quartile range (Q1-Q3)	58 to 75	60 to 70	62 to 75
Gender categorical Units: Subjects			
Female	7	16	10
Male	12	10	9
WHO Performance Status Units: Subjects			
Zero	12	13	12
One	7	13	7
Site of primary tumour Units: Subjects			
Head	17	18	13
Body/ Tail	2	8	6

Longest diameter of primary lesion			
Units: mm			
median	37	34	36
inter-quartile range (Q1-Q3)	30 to 43.1	29 to 43	26 to 45

Reporting group values	Arm D	Total	
Number of subjects	27	91	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	10	39	
From 65-84 years	17	52	
85 years and over	0	0	
Age continuous			
Units: years			
median	69		
inter-quartile range (Q1-Q3)	58 to 75	-	
Gender categorical			
Units: Subjects			
Female	11	44	
Male	16	47	
WHO Performance Status			
Units: Subjects			
Zero	10	47	
One	17	44	
Site of primary tumour			
Units: Subjects			
Head	25	73	
Body/ Tail	2	18	
Longest diameter of primary lesion			
Units: mm			
median	35		
inter-quartile range (Q1-Q3)	26 to 45	-	

End points

End points reporting groups

Reporting group title	Arm A
Reporting group description: Capecitabine (830mg/m2 oral bd) + nelfinavir + 50.4Gy in 28#	

Reporting group title	Arm B
Reporting group description: Capecitabine (830mg/m2 oral bd) + 50.4Gy in 28#	

Reporting group title	Arm C
Reporting group description: Capecitabine (830mg/m2 oral bd) + nelfinavir** + 60Gy in 30#	

Reporting group title	Arm D
Reporting group description: Capecitabine (830mg/m2 oral bd) + 60Gy in 30#	

Primary: Overall survival by radiotherapy arms (arms A+B vs arms C+D)

End point title	Overall survival by radiotherapy arms (arms A+B vs arms C+D)
End point description: An event is defined as death, patients still alive at the end of the study were censored	
End point type	Primary
End point timeframe: Time from registration to event (death).	

End point values	Arm A	Arm B	Arm C	Arm D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19	19	19	19
Units: Median overall survival				
median (confidence interval 60%)	15.1 (13.8 to 20.8)	18.2 (14.3 to 21.6)	15.6 (14.2 to 16.9)	18.4 (17.5 to 21.4)

Statistical analyses

Statistical analysis title	OS Hazard Ratio
Statistical analysis description: Overall survival by radiotherapy arms (arms A+B vs arms C+D)	
Comparison groups	Arm A v Arm B v Arm C v Arm D

Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.68 [2]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.13
Confidence interval	
level	Other: 60 %
sides	2-sided
lower limit	0.91
upper limit	1.4

Notes:

[1] - one-sided

[2] - onse-sided

Primary: Progression Free Survival by nelfinavir arms (Arms A+C vs arms B+D)

End point title	Progression Free Survival by nelfinavir arms (Arms A+C vs arms B+D)

End point description:

An event is defined as disease progression or death. Patients who had not progressed or died by the end of the study were censored.

End point type	Primary

End point timeframe:

Time from randomisation to event (disease progression or death)

End point values	Arm A	Arm B	Arm C	Arm D
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	19	19	19	19
Units: Days				
median (confidence interval 60%)	9.9 (7.8 to 10.2)	12 (10.3 to 17.6)	10.1 (9.9 to 11.6)	11.1 (9.6 to 12.8)

Statistical analyses

Statistical analysis title	PFS Hazard ratio

Statistical analysis description:

Progression Free Survival by nelfinavir arms (Arms A+C vs arms B+D)

Comparison groups	Arm A v Arm B v Arm C v Arm D
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	= 0.98
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.71

Confidence interval	
level	Other: 60 %
sides	2-sided
lower limit	1.38
upper limit	2.12

Notes:

[3] - One-sided (Arms A+C vs arms B+D)

Adverse events

Adverse events information	
Timeframe for reporting adverse events: From consent to 30 days past last treatment date	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.1
Reporting groups	
Reporting group title	Arm A
Reporting group description: Cape + Nelf + 50.4Gy (28#)	
Reporting group title	Arm B
Reporting group description: Cape + 50.4Gy (28#)	
Reporting group title	Arm C
Reporting group description: Cape + Nelf + 60.0Gy (30#)	
Reporting group title	Arm D
Reporting group description: Cape + 60.0Gy (30#)	

Serious adverse events	Arm A	Arm B	Arm C
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 19 (52.63%)	14 / 26 (53.85%)	15 / 19 (78.95%)
number of deaths (all causes)	14	17	16
number of deaths resulting from adverse events	0	0	0
Vascular disorders			
Vascular disorders			
subjects affected / exposed	0 / 19 (0.00%)	1 / 26 (3.85%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 14	0 / 17	0 / 16
General disorders and administration site conditions			
General Disorders & Administration Site Conditions			
subjects affected / exposed	4 / 19 (21.05%)	4 / 26 (15.38%)	4 / 19 (21.05%)
occurrences causally related to treatment / all	4 / 5	2 / 4	3 / 4
deaths causally related to treatment / all	0 / 14	0 / 17	0 / 16
Respiratory, thoracic and mediastinal disorders			

Respiratory, thoracic and mediastinal disorders			
subjects affected / exposed	3 / 19 (15.79%)	1 / 26 (3.85%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	3 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 14	0 / 17	0 / 16
Psychiatric disorders			
Psychiatric disorders			
subjects affected / exposed	0 / 19 (0.00%)	0 / 26 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 14	0 / 17	0 / 16
Investigations			
Investigations			
subjects affected / exposed	0 / 19 (0.00%)	0 / 26 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 14	0 / 17	0 / 16
Injury, poisoning and procedural complications			
Injury; poisoning and procedural complications			
subjects affected / exposed	0 / 19 (0.00%)	0 / 26 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 14	0 / 17	0 / 16
Blood and lymphatic system disorders			
Blood & Lymphatic System Disorders			
subjects affected / exposed	0 / 19 (0.00%)	1 / 26 (3.85%)	2 / 19 (10.53%)
occurrences causally related to treatment / all	0 / 0	0 / 1	2 / 2
deaths causally related to treatment / all	0 / 14	0 / 17	0 / 16
Gastrointestinal disorders			
Gastrointestinal Disorders			
subjects affected / exposed	1 / 19 (5.26%)	3 / 26 (11.54%)	4 / 19 (21.05%)
occurrences causally related to treatment / all	3 / 3	3 / 3	3 / 4
deaths causally related to treatment / all	0 / 14	0 / 17	0 / 16
Hepatobiliary disorders			
Hepatobiliary			
subjects affected / exposed	2 / 19 (10.53%)	1 / 26 (3.85%)	4 / 19 (21.05%)
occurrences causally related to treatment / all	0 / 2	0 / 1	2 / 5
deaths causally related to treatment / all	0 / 14	0 / 17	0 / 16

Skin and subcutaneous tissue disorders			
Skin and subcutaneous tissue disorders			
subjects affected / exposed	0 / 19 (0.00%)	0 / 26 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 14	0 / 17	0 / 16
Renal and urinary disorders			
Renal and urinary disorders			
subjects affected / exposed	0 / 19 (0.00%)	1 / 26 (3.85%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 14	0 / 17	0 / 16
Musculoskeletal and connective tissue disorders			
Musculoskeletal & Connective Tissue Disorders			
subjects affected / exposed	1 / 19 (5.26%)	0 / 26 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 14	0 / 17	0 / 16
Infections and infestations			
Infections & Infestations			
subjects affected / exposed	4 / 19 (21.05%)	7 / 26 (26.92%)	9 / 19 (47.37%)
occurrences causally related to treatment / all	2 / 6	3 / 9	3 / 10
deaths causally related to treatment / all	0 / 14	0 / 17	0 / 16
Metabolism and nutrition disorders			
Metabolism & Nutrition Disorders			
subjects affected / exposed	1 / 19 (5.26%)	0 / 26 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 14	0 / 17	0 / 16

Serious adverse events	Arm D		
Total subjects affected by serious adverse events			
subjects affected / exposed	18 / 27 (66.67%)		
number of deaths (all causes)	17		
number of deaths resulting from adverse events	0		
Vascular disorders			
Vascular disorders			

subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 17		
General disorders and administration site conditions			
General Disorders & Administration Site Conditions			
subjects affected / exposed	7 / 27 (25.93%)		
occurrences causally related to treatment / all	8 / 10		
deaths causally related to treatment / all	0 / 17		
Respiratory, thoracic and mediastinal disorders			
Respiratory, thoracic and mediastinal disorders			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 17		
Psychiatric disorders			
Psychiatric disorders			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 17		
Investigations			
Investigations			
subjects affected / exposed	2 / 27 (7.41%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 17		
Injury, poisoning and procedural complications			
Injury; poisoning and procedural complications			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 17		
Blood and lymphatic system disorders			
Blood & Lymphatic System Disorders			
subjects affected / exposed	2 / 27 (7.41%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 17		

Gastrointestinal disorders			
Gastrointestinal Disorders			
subjects affected / exposed	7 / 27 (25.93%)		
occurrences causally related to treatment / all	5 / 8		
deaths causally related to treatment / all	0 / 17		
Hepatobiliary disorders			
Hepatobiliary			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 17		
Skin and subcutaneous tissue disorders			
Skin and subcutaneous tissue disorders			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 17		
Renal and urinary disorders			
Renal and urinary disorders			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 17		
Musculoskeletal and connective tissue disorders			
Musculoskeletal & Connective Tissue Disorders			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 17		
Infections and infestations			
Infections & Infestations			
subjects affected / exposed	8 / 27 (29.63%)		
occurrences causally related to treatment / all	5 / 8		
deaths causally related to treatment / all	0 / 17		
Metabolism and nutrition disorders			
Metabolism & Nutrition Disorders			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 17		

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

Non-serious adverse events	Arm A	Arm B	Arm C
Total subjects affected by non-serious adverse events subjects affected / exposed	19 / 19 (100.00%)	26 / 26 (100.00%)	19 / 19 (100.00%)
Vascular disorders Vascular disorders subjects affected / exposed	5 / 19 (26.32%)	5 / 26 (19.23%)	6 / 19 (31.58%)
occurrences (all)	10	13	14
Surgical and medical procedures Surgical and medical procedures subjects affected / exposed	0 / 19 (0.00%)	1 / 26 (3.85%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions General Disorders & Administration Site Conditions subjects affected / exposed	18 / 19 (94.74%)	24 / 26 (92.31%)	15 / 19 (78.95%)
occurrences (all)	51	71	63
Reproductive system and breast disorders Reproductive system and breast disorders subjects affected / exposed	0 / 19 (0.00%)	0 / 26 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders Respiratory, thoracic and mediastinal disorders subjects affected / exposed	5 / 19 (26.32%)	10 / 26 (38.46%)	7 / 19 (36.84%)
occurrences (all)	8	21	8
Psychiatric disorders Psychiatric disorders subjects affected / exposed	5 / 19 (26.32%)	5 / 26 (19.23%)	1 / 19 (5.26%)
occurrences (all)	8	6	1
Investigations			

Investigations			
subjects affected / exposed	9 / 19 (47.37%)	11 / 26 (42.31%)	12 / 19 (63.16%)
occurrences (all)	38	32	70
Injury, poisoning and procedural complications			
Injury; poisoning and procedural complications			
subjects affected / exposed	0 / 19 (0.00%)	1 / 26 (3.85%)	2 / 19 (10.53%)
occurrences (all)	0	1	3
Cardiac disorders			
Cardiac Disorders			
subjects affected / exposed	1 / 19 (5.26%)	3 / 26 (11.54%)	2 / 19 (10.53%)
occurrences (all)	1	7	2
Nervous system disorders			
Nervous System Disorders			
subjects affected / exposed	14 / 19 (73.68%)	20 / 26 (76.92%)	13 / 19 (68.42%)
occurrences (all)	29	33	39
Blood and lymphatic system disorders			
Blood & Lymphatic System Disorders			
subjects affected / exposed	5 / 19 (26.32%)	12 / 26 (46.15%)	9 / 19 (47.37%)
occurrences (all)	23	33	26
Eye disorders			
Eye disorders			
subjects affected / exposed	0 / 19 (0.00%)	2 / 26 (7.69%)	3 / 19 (15.79%)
occurrences (all)	0	3	3
Gastrointestinal disorders			
Gastrointestinal Disorders			
subjects affected / exposed	15 / 19 (78.95%)	25 / 26 (96.15%)	17 / 19 (89.47%)
occurrences (all)	71	146	94
Hepatobiliary disorders			
Hepatobiliary			
subjects affected / exposed	0 / 19 (0.00%)	1 / 26 (3.85%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Skin and subcutaneous tissue disorders			
Skin and subcutaneous tissue disorders			
subjects affected / exposed	14 / 19 (73.68%)	17 / 26 (65.38%)	11 / 19 (57.89%)
occurrences (all)	29	43	24
Renal and urinary disorders			

Renal and urinary disorders			
subjects affected / exposed	3 / 19 (15.79%)	0 / 26 (0.00%)	1 / 19 (5.26%)
occurrences (all)	4	0	1
Musculoskeletal and connective tissue disorders			
Musculoskeletal & Connective Tissue Disorders			
subjects affected / exposed	5 / 19 (26.32%)	9 / 26 (34.62%)	6 / 19 (31.58%)
occurrences (all)	11	18	12
Infections and infestations			
Infections & Infestations			
subjects affected / exposed	10 / 19 (52.63%)	11 / 26 (42.31%)	9 / 19 (47.37%)
occurrences (all)	19	20	15
Metabolism and nutrition disorders			
Metabolism & Nutrition Disorders			
subjects affected / exposed	9 / 19 (47.37%)	12 / 26 (46.15%)	9 / 19 (47.37%)
occurrences (all)	11	20	27

Non-serious adverse events	Arm D		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 27 (100.00%)		
Vascular disorders			
Vascular disorders			
subjects affected / exposed	1 / 27 (3.70%)		
occurrences (all)	1		
Surgical and medical procedures			
Surgical and medical procedures			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
General Disorders & Administration Site Conditions			
subjects affected / exposed	20 / 27 (74.07%)		
occurrences (all)	43		
Reproductive system and breast disorders			
Reproductive system and breast disorders			
subjects affected / exposed	0 / 27 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal			

disorders Respiratory, thoracic and mediastinal disorders subjects affected / exposed occurrences (all)	7 / 27 (25.93%) 9		
Psychiatric disorders Psychiatric disorders subjects affected / exposed occurrences (all)	3 / 27 (11.11%) 3		
Investigations Investigations subjects affected / exposed occurrences (all)	13 / 27 (48.15%) 85		
Injury, poisoning and procedural complications Injury; poisoning and procedural complications subjects affected / exposed occurrences (all)	2 / 27 (7.41%) 2		
Cardiac disorders Cardiac Disorders subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0		
Nervous system disorders Nervous System Disorders subjects affected / exposed occurrences (all)	17 / 27 (62.96%) 23		
Blood and lymphatic system disorders Blood & Lymphatic System Disorders subjects affected / exposed occurrences (all)	13 / 27 (48.15%) 51		
Eye disorders Eye disorders subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1		
Gastrointestinal disorders Gastrointestinal Disorders subjects affected / exposed occurrences (all)	20 / 27 (74.07%) 82		
Hepatobiliary disorders			

Hepatobiliary subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0		
Skin and subcutaneous tissue disorders Skin and subcutaneous tissue disorders subjects affected / exposed occurrences (all)	18 / 27 (66.67%) 38		
Renal and urinary disorders Renal and urinary disorders subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0		
Musculoskeletal and connective tissue disorders Musculoskeletal & Connective Tissue Disorders subjects affected / exposed occurrences (all)	6 / 27 (22.22%) 6		
Infections and infestations Infections & Infestations subjects affected / exposed occurrences (all)	9 / 27 (33.33%) 11		
Metabolism and nutrition disorders Metabolism & Nutrition Disorders subjects affected / exposed occurrences (all)	7 / 27 (25.93%) 9		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 September 2015	SA001: Protocol amendment to clarify Stage 1 & 2 objectives, inclusion of safety assessment in stage 2 objectives and endpoints, changes to pregnancy and contraception requirements
27 November 2015	SA002: Change of Principal Investigator
20 February 2018	SA003: (Protocol V6.0) Updates to all areas of protocol following Stage 1 completion including: adjustments to eligibility criteria, MTD declaration, time-point numbering. Update to Radiation Risk Assessment (higher overall dose), Updated SmPC for Capecitabine, Viracept (US and Canadian version) , IB for Nab-Paclitaxel submitted. Amended labels for Nelfinavir and Nab-Paclitaxel submitted. Updated PIS Stage1, Stage 2, Consent Form Stage 2, and Patient diary Stage 2, GP letters Stage 2 all updated. New Stage 2 sites added. Change of PI at Leeds.
06 March 2018	SA004: Update to PIS Stage 2 V5.0_10Oct2017 (as submitted with SubAmend003) to include details of GFR tests and risk of radiation exposure in order to obtain ARSAC approval for the trial.
11 May 2018	SA006: Addition of 2 new sites; The Clatterbridge Cancer Centre NHS Foundation Trust and Nottingham University Hospitals NHS Trust . Change in Principal Investigator
22 May 2018	SA005: Correction to number of CT scans in Radiation Risk Assessment in REC form (Part B, Section 3). Number of CT scans to be corrected back from 4 to 5. Total radiation dose has been re-calculated.
29 November 2018	SA007: Addition of 3 new sites; Milton Keynes Hospital NHS Foundation Trust, United Lincolnshire Hospitals Trust and Taunton and Somerset NHS Foundation Trust. Change in Principal Investigators
02 April 2019	SA009: Change in Principal Investigator at NHS Grampian
28 October 2019	SA008: Protocol version 7.0- reduction in sample size, removal of arm E. Option for patients to begin treatment on dose level -1.
28 April 2020	SA010: Protocol V8.0 Notification of temporary recruitment halt and Urgent Safety Measure
28 April 2020	SA011: Request to lift temporary recruitment halt

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date

24 February 2020	Urgent Safety Measure implemented due to lack of efficacy of the IMP nelfinavir (identified by IDMC & approved by the TSC) , affecting arms A & C. No safety concerns regarding nelfinavir. Recruitment paused to prevent further randomisations to arms A & C. Registered patients were able to continue on the trial but were randomised to arms B or D only. Recruitment was never re-started due to the COVID-19 pandemic but patients already enrolled continued on trial treatment as per protocol V8.0.	-

Notes:

Limitations and caveats

None reported