		Arm A N = 19	Arm B N = 26	Arm C N = 19	Arm D N = 27	All randomised to A-D N = 91	Arm E N = 15	Observation cohort + early withdrawals N = 53	All registered N = 159
Registration									
Sex	Female	7 (36.8)	16 (61.5)	10 (52.6)	11 (40.7)	44 (48.4)	6 (40)	23 (43.4)	73 (45.9)
	Male	12 (63.2)	10 (38.5)	9 (47.4)	16 (59.3)	47 (51.6)	9 (60)	30 (56.6)	86 (54.1)
Age		70 [58, 75]	62.5 [60, 70]	69 [62, 72]	69 [58, 75]	68 [59, 72]	65 [59, 69]	69 [63, 75]	68 [60, 73]
WHO PS	0	12 (63.2)	13 (50)	12 (63.2)	10 (37)	47 (51.6)	7 (46.7)	16 (30.2)	70 (44)
	1	7 (36.8)	13 (50)	7 (36.8)	17 (63)	44 (48.4)	8 (53.3)	37 (69.8)	89 (56)
Site of primary tumour	Head	17 (89.5)	18 (69.2)	13 (68.4)	25 (92.6)	73 (80.2)	11 (73.3)	40 (75.5)	124 (78)
	Body/tail	2 (10.5)	8 (30.8)	6 (31.6)	2 (7.4)	18 (19.8)	4 (26.7)	13 (24.5)	35 (22)
Longest primary lesion diameter (mm)		37 [30, 43.1]	34 [29, 43]	36 [34, 47]	35 [26, 45]	36 [30, 45]	37 [25, 46]	42 [34, 50.5]	37 [30.3, 46]
CA19-9 concentration at C1D1 (U/mL)		915.5 [61, 2124]	412.5 [98, 1372.5]	664 [181, 2256]	161.5 [41.6, 1212.5]	459 [94, 1587]	322 [129, 1184]	218 [56, 2018]	404 [88, 1535]
No. of days from staging CT to registration		16 [6, 26]	11.5 [5, 23]	8 [5, 11]	14 [5, 32]	11 [6, 21]	16 [7, 26]	12 [6, 28]	12 [6, 26]
No. of days from registration to start of induction chemotherapy		8 [5, 13]	3 [1, 6]	6 [1, 11]	4 [2, 8]	6 [2, 8]	5 [2, 11]	6 [2, 11]	6 [2, 9]
Randomisation									
WHO PS at randomisation	0	3 (15.8)	5 (19.2)	5 (26.3)	4 (14.8)	17 (18.7)	2 (13.3)		
	1	16 (84.2)	21 (80.8)	14 (73.7)	23 (85.2)	74 (81.3)	13 (86.7)		
Longest primary lesion diameter (mm)		28 [19, 40.5]	32 [24, 36]	35.5 [25, 43]	33.6 [22, 41]	32.5 [24, 41]	32 [20, 45]		
CA19-9 concentration at C1D1 (U/mL)		85.5 [25, 305.5]	54 [25.2, 467]	238 [50, 539]	56 [26, 124]	95 [30, 325]	117 [36, 421]		
No. of days from registration to start of chemoradiotherapy		132 [127.5, 148]	133 [128, 140]	137 [130, 147]	133 [126, 147]	133.5 [127.5, 146.5]			
Withdrew before start of chemoradiotherapy		3 (15.8)	2 (7.7)	3 (15.8)	4 (14.8)	11 (12.1)			

Table 1: Baseline patient and tumour characteristics for patients enrolled in stage 2 of the SCALOP-2 trial. Data are n (%) or median (lower quartile, upper quartile). Where the numbers with available data are different to the column total, the numbers included is indicated by (n=). The minimisation factors were WHO PS at randomisation and site of primary tumour. Arm E was initially planned as a calibration arm but was closed to recruitment in November 2019 due to the availability of other reference data. [1]There are missing data in these variables. [2]If more than one result is available from different imaging modalities

(e.g. CT and MRI), the longest measurement is taken. CnDn expresses the gemcitabine/nab-paclitaxel cycle number (Cn) and the specific day (Dn) of that cycle on which the measurement was recorded.

	Arm A n= 19	**Arm B** n= 26	**Arm C** n= 19	**Arm D** n= 27	**Arms A-D total** n= 91	**Arms A+C (CRT +nelfinavir)** n=38	**Arms B+D (CRT - nelfinavir)** (n=38, *up to arm A and C closure*)
Withdrew before starting CRT n (%)	**3 (15.8)**	**2 (7.7)**	**3 (15.8)**	**4 (14.8)**	**12 (13.2)**	**6 (15.8)**	**3 (7.9)**
Started CRT	**16 (84.2)**	**24 (92.3)**	**16 (84.2)**	**23 (85.2)**	**79 (86.8)**	**32 (84.2)**	**35 (92.1)**
Completed CRT – unaltered	7 (43.8)	13 (54.2)	6 (37.5)	14 (60.9)	40 (50.6)	13 (40.6)	18 (51.4)
Completed CRT – treatment altered	8 (50)	10 (41.7)	10 (62.5)	9 (39.1)	37 (46.8)	18 (56.3)	16 (45.7)
Early withdrawal*	1 (6.3)	1 (4.2)	0 (0)	0 (0)	2 (2.5)	1 (3.1)	1 (2.9)
Capecitabine (prescribed dose = 830mg/m2)**							
Completed >80%	13 (81.3)	19 (79.2)	13 (81.3)	21 (91.3)	66 (83.5)	26 (81.3%)	30 (85.7)
Completed 100%	*10 (62.5)*	*13 (54.2)*	*10 (62.5)*	*14 (60.9)*	*47 (59.05)*	*20 (62.5)*	*18 (51.4)*
Completed >80% to <100%	*3 (18.8)*	*6 (25)*	*3 (18.8)*	*7 (30.4)*	*19 (24.1)*	*6 (18.8)*	*12 (34.3)*
Completed <80%	3 (18.8)	4 (16.7)	3 (18.8)	2 (8.7)	12 (15.2)	6 (18.8)	4 (11.4)
Nelfinavir (prescribe dose = 1250mg)							
Completed >70%	12 (75)	NA	11 (68.8)	NA	23 (20.1)	23 (71.9)	*NA*
Completed 100%	*10 (62.5)*	*NA*	*9 (56.3)*	*NA*	*19 (24.1)*	*19 (59.4)*	*NA*
Completed >70% to <100%	*2 (12.5)*	*NA*	*2 (12.5)*	*NA*	*4 (5.1)*	*4 (12.5)*	NA
Completed <70%	3 (18.8)	NA	3 (18.8)	NA	6 (7.6)	6 (18.8)	NA
Nelfinavir discontinued pre-CRT	1 (6.3)	NA	2 (12.5)	NA	3 (3.8)	3 (8.6)	NA
Radiotherapy (protocol dose= 50.4Gy in 28# or 60.0Gy in 30#)							
Completed full protocol dose: 28# (arms A/B) or 30# (arms C/D)	15 (93.8)	23 (95.8)	16 (100)	23 (100)	77 (97.5)	31 (96.9)	34 (97.1)
Completed 25-27# (arms A/B) or 28-29# (arms C/D)	0 (0)	0 (0)0	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Completed 1-24# (arms A/B) or 1-27# (arms C/D)	1 (6.3)	1 (4.2)	0 (0)	0 (0)	2 (2.5)	1 (3.1)	1 (2.9)

Table 2: Compliance with specific components of chemoradiotherapy by treatment arm. Data are n (%). Denominator is all patients for 'Withdrew before starting CRT' and 'Started CRT'. Subsequent denominator for all other categories is the total number of patients who started CRT. *One patient withdrew

from arm A with suspected new onset dementia and one patient chose to withdraw from arm B with no other reason specified. **Data not known (patient diary lost) for one patient in arm B, representing 4.2% of this cohort.

	50.4 Gy in 28# (n= 45)		60 Gy in 30# (n= 46)		Total (n = 91)	
Grade:	**1-5**	**3-4**	**1-5**	**3-4**	**1-5**	**3-4**
Haematological						
Anaemia	3 (6.7)	0 (0)	4 (8.7)	0 (0)	7 (7.7)	0 (0)
Thrombocytopenia	1 (2.2)	0 (0)	1 (2.2)	0 (0)	2 (2.2)	0 (0)
Neutropenia	1 (2.2)	1 (2.2)	0 (0)	0 (0)	1 (1.1)	1 (1.1)
Gastrointestinal						
Duodenal obstruction	1 (2.2)	1 (2.2)	0 (0)	0 (0)	1 (1.1)	1 (1.1)
Abdominal pain	0 (0)	0 (0)	1 (2.2)	1 (2.2)	1 (1.1)	1 (1.1)
Vomiting	1 (2.2)	1 (2.2)	0 (0)	0 (0)	1 (1.1)	1 (1.1)
General						
Pyrexia	1 (2.2)	0 (0)	0 (0)	0 (0)	1 (1.1)	0 (0)
Hepatobiliary						
Cholangitis	1 (2.2)	1 (2.2)	1 (2.2)	1 (2.2)	2 (2.2)	2 (2.2)
Cholecystitis	0 (0)	0 (0)	1 (2.2)	1 (2.2)	1 (1.1)	1 (1.1)
Bile duct obstruction	1 (2.2)	1 (2.2)	0 (0)	0 (0)	1 (1.1)	1 (1.1)
Infections						
Influenza	0 (0)	0 (0)	1 (2.2)	1 (2.2)	1 (1.1)	1 (1.1)
Stoma site infection	1 (2.2)	1 (2.2)	0 (0)	0 (0)	1 (1.1)	1 (1.1)
Lower respiratory tract infection	1 (2.2)	1 (2.2)	0 (0)	0 (0)	1 (1.1)	1 (1.1)
Gastroenteritis	1 (2.2)	1 (2.2)	0 (0)	0 (0)	1 (1.1)	1 (1.1)
Respiratory						
Interstitial lung disease	1 (2.2)	1 (2.2)	0 (0)	0 (0)	1 (1.1)	1 (1.1)

Table 3: A summary of adverse events reported during chemoradiotherapy, subdivided by trial arms and grade of severity. Only one patient, who was in the high-dose CRT arm, experienced an adverse event related to nelfinavir.

	60.0 Gy RT in 30# Arms C+D (n=46*, n=38**)	50.4 Gy RT in 28# Arms A+B (n=45*, n=38**)	CRT +nelfinavir Arms A+C (n=38*, n=38**)	CRT -nelfinavir Arms B+D (n=53*, n=38**)
	Progression-free survival		Overall survival	
Numbers included	46	45	38	38
No. events n (%)	39 (84.8)	36 (80)	30 (78.9)	28 (73.7)
Median survival (60% CI)	10.5 (10.1-11.8)	10.3 (10.0-11.9)	15.1 (14.2-16.4)	18.4 (17.5-21.4)
Log-rank p-value***	0.87		0.97	
Adjusted HR (60% CI), p-value***	1.26 (1.03-1.55), 0.83		1.71 (1.35- 2.16), 0.97	
Local progression by 12 months				
Local progression (with or without metastasis)	11 (23.9)	15 (33.3)	12 (31.6)	11 (28.9)
Metastasis with no local progression	16 (34.8)	11 (24.4)	15 (39.5)	9 (23.7)
Progression- free with <12 months follow-up	1 (2.2)	1 (2.2)	0	0
Progression-free at 12 months	18 (39.1)	18 (40)	11 (28.9)	18 (47.4)
Resection rate after randomisation				
No. resections n (%)	4 (8.7)	6 (13.3)	4 (10.5)	5 (13.2)
Chi-squared p-value	0.48		0.72	
CA19-9 level (U/mL)				
Start of CRT	n=36	n=37	n= 32	n= 33
Median [LQ, UQ]	38.7 [15, 84.3]	40 [18, 204]	57 [16, 167.5]	38 [16, 87.5]
6 weeks post CRT	n= 34	n=31	n= 28	n= 27
Median [LQ, UQ]	42.0 [19, 144]	18 [8, 357]	54 [13, 524.5]	27 [11, 72.8]
Median change (95% CI)	n=31	n=29	n= 28	n= 26
	5 (-2.8-23.0)	0 (-11.6-10.4)	9.6 (0-253.9)	-2.3 (-12.1, 8.8)
Disease response rate at 6 weeks post-CRT				
Scan done n (%)	37 (80.4)	39 (86.7)	32(84.2)	33 (86.8)
Complete response n (%)	2 (4.4)	2 (4.4)	2 (5.3)	2 (5.3)
Partial response n (%)	4 (8.7)	8 (17.8)	6 (15.8)	5 (13.2)
Stable disease n (%)	23 (50.0)	12 (26.7)	12 (31.6)	17 (44.7)
Progressive disease n (%)	6 (13.0)	14 (31.1)	11 (29.0)	7 (18.4)
Not evaluable n (%)	2 (4.4)	3 (6.7)	1 (2.6)	2 (5.3)

Table 4: A summary of secondary endpoints relating to disease control measures. *Number randomised. **Number randomised before closure of arms A and C. ***One-sided value