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Citation for final published version:

Mukherjee, Somnath, Qi, Cathy, Shaw, Rachel, Jones, Christopher M., Bridgewater, John A., Radhakrishna, Ganesh, Patel, Neel, Holmes, Jane, Virdee, Pradeep S., Tranter, Bethan, Parsons, Philip, Falk, Stephen, Wasan, Harpreet S., Ajithkumar, Thankamma V., Holyoake, Daniel, Roy, Rajarshi, Scott-Brown, Martin, Hurt, Christopher N., O'Neill, Eric, Sebag-Montefiore, David, Maughan, Tim S., Hawkins, Maria A. and Corrie, Pippa 2024. Standard or high dose chemoradiotherapy, with or without the protease inhibitor nelfinavir, in patients with locally advanced pancreatic cancer: The phase 1/randomised phase 2 SCALOP-2 trial. *European Journal of Cancer* 209 , 114236. 10.1016/j.ejca.2024.114236

Publishers page: <http://dx.doi.org/10.1016/j.ejca.2024.114236>

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		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. ¹There are missing data in these variables. ²If 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.

Grade:	50.4 Gy in 28# (n= 45)		60 Gy in 30# (n= 46)		Total (n = 91)	
	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 5 (-2.8-23.0)	n=29 0 (-11.6-10.4)	n= 28 9.6 (0-253.9)	n= 26 -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