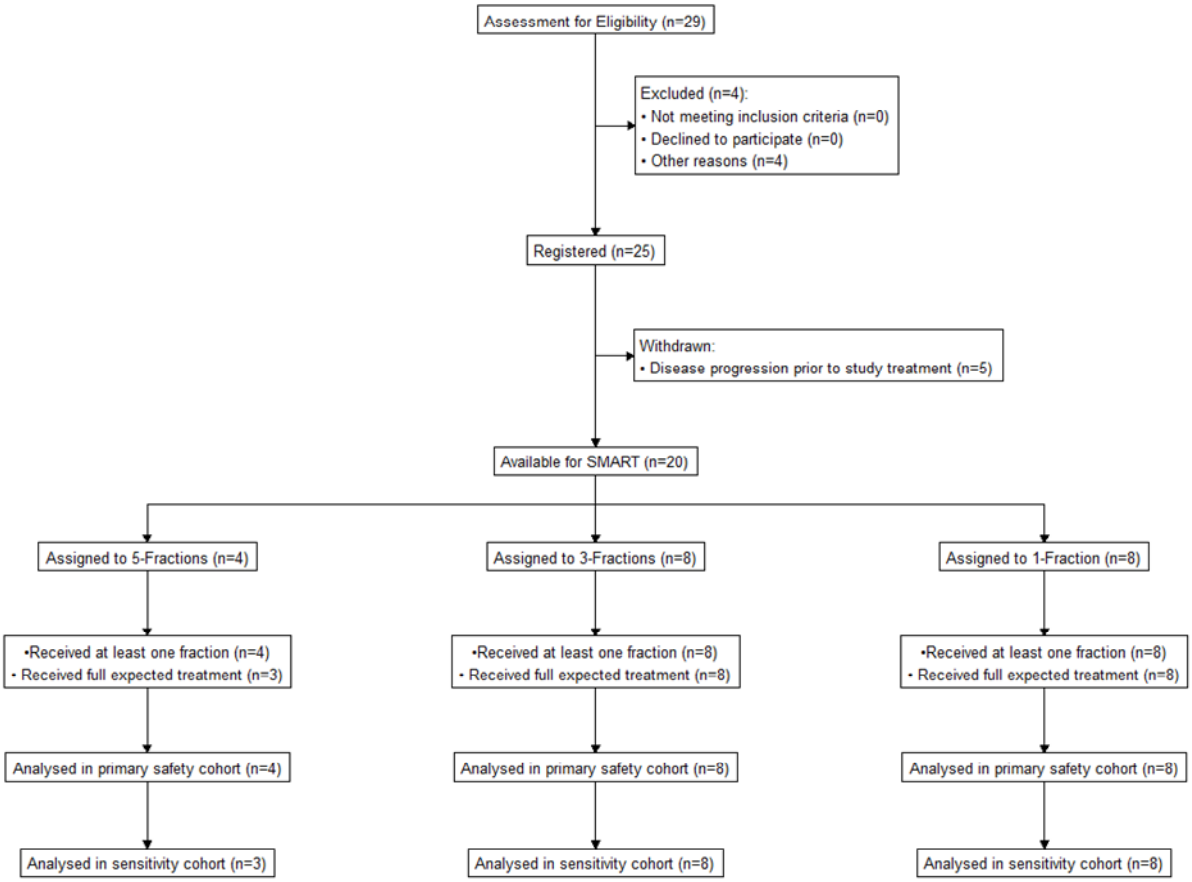
EMERALD ISRCTN10557832 Basic Results Summary

1. Participant Flow



2. Baseline characteristics

	5-Fractions (n=4)	3-Fractions (n=8)	1-Fraction (n=8)	Total (n=20)
Age (Years)	n=4, 69.8 (8.5)	n=8, 76.0 (8.4)	n=8, 67.2 (8.8)	n=20, 71.2 (9.1)
Time since diagnosis (months)	n=4, 7.3 (0.5)	n=8, 9.1 (5.4)	n=8, 12.8 (10.4)	n=20, 10.3 (7.5)
Diameter of target lesion (mm)	n=3, 29.7 (21.0)	n=5, 32.8 (10.7)	n=5, 31.0 (15.9)	n=13, 31.4 (14.1)
Standardised uptake value	n=1, 7.0 (-)	n=0, - (-)	n=1, 5.0 (-)	n=2, 6.0 (1.4)

	5-Fractions (n=4)	3-Fractions (n=8)	1-Fraction (n=8)	Total (n=20)
(SUV) of target lesion				
CA 19-9 (U/mL)	n=4, 126.0 (148.3)	n=7, 39.4 (70.2)	n=8, 611.4 (706.4)	n=19, 298.5 (525.0)
Sex				
Male	2 (50.0)	5 (62.5)	1 (12.5)	8 (40.0)
Female	2 (50.0)	3 (37.5)	7 (87.5)	12 (60.0)
Carcinoma Diagnosis Confirmation Method*				
Histologically	0 (0.0)	5 (62.5)	4 (50.0)	9 (45.0)
Cytologically	3 (75.0)	2 (25.0)	3 (37.5)	8 (40.0)
MDT confirmed	1 (25.0)	1 (12.5)	2 (25.0)	4 (20.0)
The first site of target tumour with pancreas				
Head	2 (50.0)	4 (50.0)	6 (75.0)	12 (60.0)
Body or Tail	2 (50.0)	1 (12.5)	0 (0.0)	3 (15.0)
Local recurrence	0 (0.0)	3 (37.5)	2 (25.0)	5 (25.0)
Tumour Resectability				
Missing	0 (0.0)	2 (25.0)	2 (25.0)	4 (20.0)
Resectable but medically inoperable	0 (0.0)	2 (25.0)	2 (25.0)	4 (20.0)
Unresectable	4 (100.0)	4 (50.0)	4 (50.0)	12 (60.0)
Previous chemotherapy?				
Yes	4 (100.0)	7 (87.5)	8 (100.0)	19 (95.0)
No	0 (0.0)	1 (12.5)	0 (0.0)	1 (5.0)
Number of previous chemotherapy lines received				
1	4 (100.0)	7 (100.0)	7 (87.5)	18 (90.0)
2	0 (0.0)	0 (0.0)	1 (12.5)	1 (5.0)

	5-Fractions (n=4)	3-Fractions (n=8)	1-Fraction (n=8)	Total (n=20)
Previous chemotherapy response				
Responded	1 (25.0)	0 (0.0)	0 (0.0)	1 (5.0)
Stable	2 (50.0)	4 (50.0)	8 (100.0)	14 (70.0)
Local progression	1 (25.0)	2 (25.0)	0 (0.0)	3 (15.0)
No previous chemotherapy	0 (0.0)	1 (12.5)	0 (0.0)	1 (5.0)
Missing	0 (0.0)	1 (12.5)	0 (0.0)	1 (5.0)
Latest line of previous chemotherapy				
Gemcitabine	0 (0.0)	1 (12.5)	0 (0.0)	1 (5.0)
Gemcitabine and Capecitabine (or 5FU)	0 (0.0)	1 (12.5)	1 (12.5)	2 (10.0)
Oxaliplatin and Capecitabine (or 5FU)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
FOLFIRINOX (5FU, Oxaliplatin, Irinotecan, Folinic Acid)	4 (100.0)	5 (62.5)	6 (75.0)	15 (75.0)
Irinotecan and 5FU (or Capecitabine)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	1 (12.5)	1 (5.0)
No previous chemotherapy	0 (0.0)	1 (12.5)	0 (0.0)	1 (5.0)
ECOG				
0	3 (75.0)	4 (50.0)	7 (87.5)	14 (70.0)
1	1 (25.0)	4 (50.0)	1 (12.5)	6 (30.0)

*Each patient could be confirmed by multiple carcinoma diagnosis confirmation methods.

3. OUTCOME MEASURES

Primary Outcome Measure		DLT within 3 months from the start of MRgRT				
Fractionation Regimen	**Number of patients included in primary analysis**	**Number of DLTs observed**	**Observed DLT rate**	**Regimen safe**	**Posterior probability of the DLT rate being above 0.15**	**95% Credible interval***
5-Fractions	4	0	0	Yes	0.167	(0.002,0.285)
3-Fractions	8	0	0	Yes	0.087	(0.002,0.218)
1-Fraction	8	0	0	Yes	0.087	(0.002,0.218)

1.1A Secondary Outcome Measure (Overall Survival)

	5-Fractions (N=4)		**3-Fractions (N=8)**		**1-Fraction (N=8)**		**Total (N=20)**	
	Event/n	Survival rate (%)	Event/n	Survival rate (%)	Event/n	Survival rate (%)	Event/n	Survival rate (%)
12 months overall survival from start of RT	2/4	37.5	1/8	85.7	3/8	52.5	6/20	62.9
12 months overall survival from date of diagnosis	1/4	75	0/8	100	0/8	100	1/20	94.7
18 months overall survival from start of RT	2/4	37.5	1/8	85.7	4/8	26.2	7/20	50.3
24 months overall survival from date of diagnosis	2/4	37.5	1/8	85.7	4/8	42.9	7/20	56.2

1.1B Secondary Outcome Measure (Progression Free Survival)								
	5-Fractions (N=4)		3-Fractions (N=8)		1-Fraction (N=8)		Total (N=20)	
	Event/n	Survival rate (%)	Event/n	Survival rate (%)	Event/n	Survival rate (%)	Event/n	Survival rate (%)
12 months progression free survival from start of RT	2/4	50	2/8	85.7	3/8	56.2	7/20	62.3
12 months progression free survival from date of diagnosis	2/4	50	0/8	100	1/8	87.5	3/20	84.2
18 months progression free survival from start of RT	2/4	50	2/8	72.9	4/8	28.1	8/20	49.8
24 months progression free survival from date of diagnosis	2/4	50	2/8	71.4	4/8	43.8	8/20	53.2

1.2 Secondary Outcome Measure (Freedom from Local Progression)								
	5-Fractions (N=4)		3-Fractions (N=8)		1-Fraction (N=8)		Total (N=20)	
	Event/n	Survival rate (%)	Event/n	Survival rate (%)	Event/n	Survival rate (%)	Event/n	Survival rate (%)
12 months local progression free survival from start of RT	2/4	50	2/8	72.9	3/8	56.2	7/20	62.3
12 months local progression free survival from date of diagnosis	2/4	50	0/8	100	1/8	87.5	3/20	84.2
18 months local progression free survival from start of RT	2/4	50	2/8	72.9	4/8	28.1	8/20	49.8

1.2 Secondary Outcome Measure (Freedom from Local Progression)								
	5-Fractions (N=4)		3-Fractions (N=8)		1-Fraction (N=8)		Total (N=20)	
	Event/n	Survival rate (%)	Event/n	Survival rate (%)	Event/n	Survival rate (%)	Event/n	Survival rate (%)
24 months local progression free survival from date of diagnosis	2/4	50	2/8	71.4	4/8	43.8	8/20	53.2

1.3 Secondary Outcome Measure (Freedom from Metastatic Progression)				
	5-Fractions (n=4)	3-Fractions (n=8)	1-Fraction (n=8)	Total (n=20)
Disease progression				
Yes	1 (25.0)	3 (37.5)	2 (25.0)	6 (30.0)
No	3 (75.0)	5 (62.5)	6 (75.0)	14 (70.0)
Progression Diagnosis Method				
Clinical examination	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
CT/MRI/FDG PET scan	1 (25.0)	3 (37.5)	2 (25.0)	6 (30.0)
CA19-9	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Did not progress	3 (75.0)	5 (62.5)	6 (75.0)	14 (70.0)
Progression Site (Possible to Progress in Multiple Sites)				
Local progression within the primary tumour	1 (25.0)	3 (37.5)	2 (25.0)	6 (30.0)
Loco-regional progression with new lesions outside the primary tumour	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

1.3 Secondary Outcome Measure (Freedom from Metastatic Progression)				
	5-Fractions (n=4)	**3-Fractions (n=8)**	**1-Fraction (n=8)**	**Total (n=20)**
Distant metastases	0 (0.0)	0 (0.0)	1 (12.5)	1 (5.0)
Did not progress	3 (75.0)	5 (62.5)	6 (75.0)	14 (70.0)
Distant metastases Site (Possible to have Multiple)				
Liver	0 (0.0)	0 (0.0)	1 (12.5)	1 (5.0)
Lung	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Peritoneum	0 (0.0)	0 (0.0)	1 (12.5)	1 (5.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
No distant metastases	4 (100.0)	8 (100.0)	7 (87.5)	19 (95.0)

Secondary Outcome Measure 2. Definitive resection rate for those undergoing surgery: N/A (there was no surgery observed).

Secondary Outcome Measure 3.1 Long term toxicity rates (specifically related to SBRT)				
	5-Fractions (N=4 patients)	**3-Fractions (N=8 patients)**	**1-Fraction (N=8 patients)**	**Total (N=20 patients)**
Number of Adverse Events	19	17	48	84
Number of Adverse Events CTCAE Grade 3+	5	3	4	12
Number of patients with adverse events	3	6	8	17
CTCAE Grade				
1	6 (31.6)	9 (52.9)	34 (70.8)	49 (58.3)
2	8 (42.1)	5 (29.4)	10 (20.8)	23 (27.4)
3	5 (26.3)	3 (17.6)	3 (6.2)	11 (13.1)
4	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Secondary Outcome Measure 3.1 Long term toxicity rates (specifically related to SBRT)				
	5-Fractions (N=4 patients)	**3-Fractions (N=8 patients)**	**1-Fraction (N=8 patients)**	**Total (N=20 patients)**
5	0 (0.0)	0 (0.0)	1 (2.1)	1 (1.2)
RT Relatedness				
Definitely Related	3 (15.8)	4 (23.5)	24 (50.0)	31 (36.9)
Probably Related	3 (15.8)	7 (41.2)	11 (22.9)	21 (25.0)
Possibly Related	9 (47.4)	3 (17.6)	5 (10.4)	17 (20.2)
Probably Not Related	1 (5.3)	0 (0.0)	0 (0.0)	1 (1.2)
Definitely Not Related	3 (15.8)	3 (17.6)	8 (16.7)	14 (16.7)
Time to resolve (days)*	n=11, 27.5 (40.0)	n=11, 19.4 (29.9)	n=32, 9.4 (11.3)	n=54, 15.1 (24.5)
Late-onset severe MRgRT toxicity				
Yes	0 (0.0)	0 (0.0)	1 (2.1)	1 (1.2)
No	6 (31.6)	2 (11.8)	2 (4.2)	10 (11.9)
N/A; Outside Late-onset severe toxicity period	13 (68.4)	15 (88.2)	45 (93.8)	73 (86.9)

*Summaries are n, mean (SD); n means the number of events.

Secondary Outcome Measure 3.2 Late GI Adverse Events >Grade 2 >12 weeks after start of MRgRT								
	5-Fractions (N=4)		**3-Fractions (N=8)**		**1-Fraction (N=8)**		**Total (N=20)**	
	Number of events (n=6)	**Number of patients (n=1)**	**Number of events (n=3)**	**Number of patients (n=3)**	**Number of events (n=3)**	**Number of patients (n=1)**	**Number of events (n=12)**	**Number of patients (n=5)**
System Organ Class								
Gastrointestinal Disorders	0 (0.0)	0 (0.0)	3 (100.0)	3 (100.0)	2 (66.7)	4 (400.0)	5 (41.7)	1 (20.0)
Hepatobiliary	1 (16.7)	1 (100.0)	0 (0.0)	0 (0.0)	1 (33.3)	2 (200.0)	2 (16.7)	1 (20.0)
Investigations	4 (66.7)	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)	4 (33.3)	0 (0.0)

Secondary Outcome Measure 3.2 Late GI Adverse Events >Grade 2 >12 weeks after start of MRgRT

	5-Fractions (N=4)		3-Fractions (N=8)		1-Fraction (N=8)		Total (N=20)	
	Number of events (n=6)	Number of patients (n=1)	Number of events (n=3)	Number of patients (n=3)	Number of events (n=3)	Number of patients (n=1)	Number of events (n=12)	Number of patients (n=5)
Musculoskeletal & Connective Tissue Disorders	1 (16.7)	1 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)	1 (8.3)	0 (0.0)

Secondary Outcome Measure 4. Freedom from further line chemotherapy				
	5-Fractions (n=4)	3-Fractions (n=8)	1-Fraction (n=8)	Total (n=20)
Post-MRgRT Chemotherapy				
Yes	1 (25.0)	0 (0.0)	0 (0.0)	1 (5.0)
No	3 (75.0)	8 (100.0)	8 (100.0)	19 (95.0)
Regimen				
Gemcitabine	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Gemcitabine and Capecitabine (or 5FU)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Oxaliplatin and Capecitabine (or 5FU)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
FOLFIRINOX (5FU, Oxaliplatin, Irinotecan, Folinic Acid)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Irinotecan and 5FU (or Capecitabine)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	1 (25.0)	0 (0.0)	0 (0.0)	1 (5.0)
Did not have Post-MRgRT chemotherapy	3 (75.0)	8 (100.0)	8 (100.0)	19 (95.0)
Intent				

Secondary Outcome Measure 4. Freedom from further line chemotherapy				
	5-Fractions (n=4)	**3-Fractions (n=8)**	**1-Fraction (n=8)**	**Total (n=20)**
Adjuvant/maintenance	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Palliative	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Did not have Post-MRgRT chemotherapy	3 (100.0)	8 (100.0)	8 (100.0)	19 (95.0)
Time from completion of radiotherapy to start of further chemotherapy (days)	n=1, 281.0 (-)	n=0, - (-)	n=0, - (-)	n=1, 281.0 (-)

4. Adverse Events

Serious Adverse Events

Patient	Fractionation Regimen	MedDRA Preferred Term	System Organ Class	Grade	RT Causality	MRI Causality	Late onset	Outcome	Time to resolve (days)	DLT	SUSAR
EM-111	5	Jaundice cholestatic	Hepatobiliary	3	Possibly Related	Definitely Not Related	No	Resolved	96	No	No
EM-118	1	Haematemesis	Gastrointestinal Disorders	5	Possibly Related	Definitely Not Related	Yes	Fatal	1	N/A; Outside DLT period	Yes

Adverse events system organ class & fractions

	5-Fractions (N=4)		3-Fractions (N=8)		1-Fraction (N=8)		Total (N=20)	
	Number of events (n=19)	**Number of patients (n=3)**	**Number of events (n=17)**	**Number of patients (n=6)**	**Number of events (n=48)**	**Number of patients (n=8)**	**Number of events (n=84)**	**Number of patients (n=17)**
System Organ Class								
Ear and labyrinth disorders	0 (0.0)	0 (0.0)	1 (5.9)	1 (16.7)	0 (0.0)	0 (0.0)	1 (1.2)	1 (5.9)
Eye disorders	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.1)	1 (12.5)	1 (1.2)	1 (5.9)
Gastrointestinal Disorders	11 (57.9)	3 (100.0)	7 (41.2)	4 (66.7)	27 (56.2)	8 (100.0)	45 (53.6)	15 (88.2)
General Disorders & Administration Site Conditions	0 (0.0)	0 (0.0)	8 (47.1)	5 (83.3)	16 (33.3)	8 (100.0)	24 (28.6)	13 (76.5)
Hepatobiliary	2 (10.5)	2 (66.7)	0 (0.0)	0 (0.0)	1 (2.1)	1 (12.5)	3 (3.6)	3 (17.6)
Infections & Infestations	1 (5.3)	1 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	1 (5.9)
Investigations	4 (21.1)	1 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (4.8)	1 (5.9)
Musculoskeletal & Connective Tissue Disorders	1 (5.3)	1 (33.3)	1 (5.9)	1 (16.7)	1 (2.1)	1 (12.5)	3 (3.6)	3 (17.6)
Nervous System Disorders	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.1)	1 (12.5)	1 (1.2)	1 (5.9)
Skin and subcutaneous tissue disorders	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.1)	1 (12.5)	1 (1.2)	1 (5.9)