SUPPLEMENTARY MATERIAL TO:

Combined analysis of the FOXFIRE, SIRFLOX and FOXFIRE-Global prospective randomised studies of first-line selective internal radiotherapy in patients with liver metastases from colorectal cancer.

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Supplementary Methods:

Permitted dose reductions/interruptions

The FOXFIRE Trial Protocol stated the following:

As this is an 'intention to treat' study, empirical dosage modifications to chemotherapy in line with standard clinical care are acceptable. The justification for the dose modification should be noted in the patient hospital records and recorded on the relevant case report form (CRF). The toxicity of each cycle of chemotherapy must be recorded before the administration of the next one and graded according to the current version of the Common Terminology Criteria for Adverse Events (CTCAE) V3.0.
Dose modifications will be made according to the worst toxicity observed during the previous cycle. Treatment should be delayed until full recovery of stomatitis or diarrhoea, and recovery to ≤CTCAE grade 2 skin or other toxicity. Blood counts should have recovered to:
Neutrophils $> 1.0 \times 10^9/L$
Platelets $> 75 \times 10^9/L$
The recommended initial dose modifications in the event of toxicity due to OxMdG chemotherapy are detailed in the following tables. Subsequent dose modifications can be made by reducing the concentration of the active constituents by 25%. All treatment modifications should be documented on the Treatment Form CRF.

Table: Recommended Dose Modification due to OxMdG Toxicity (excluding neurosensory toxicity)

Type of Toxicity (CTCAE)	**Initial Doses (mg/m²/cycle)**		
	5-FU IV bolus	5-FU IV continuous infusion	Oxaliplatin
	400	**2400**	**85**
	Dose modifications of study drugs (mg/m²/cycle) *(LV dose should not be modified)*		
Haemoglobin (any grade)	None	None	none
White blood cells (any grade)	None	None	none
Neutrophils grade 3 or 4	300	1800	65
Platelets grade 3 or 4	300	1800	65
Nausea and/or vomiting grade 4 despite adequate anti-emetic treatment	Stop treatment. Patient off study due to toxicity		
Diarrhoea grade 3	300	1800	none
Diarrhoea grade 4*	300	1800	65
Stomatitis grade 3	300	1800	none
Stomatitis grade 4*	300	1800	65
Heart ≥ grade 2	Stop treatment. Patient off study due to toxicity		
Skin grade 3 or 4	300	1800	None
Allergy grade 3 or 4	Stop treatment. Patient off study due to toxicity		
Neurocerebellar	Stop treatment. Patient off study due to toxicity		
Neurosensory: specific adaptation according to symptomatology	None	None	As described in table below
Alopecia (any grade)	None	None	None
Local Intolerance (any grade)	None	None	None
Other toxicity clearly drug related: - grade 1 or 2 - grade 3 - grade 4	 none 300 Stop treatment	 none 1800 Stop treatment	 none 65 Stop treatment

*or repeated grade 3 after 5-FU dose reduction

The oxaliplatin dose should be reduced in the next cycle according to the specific grade of peripheral neuropathy observed after a given cycle of chemotherapy (see following table).

Table: Dose Modification of Oxaliplatin Due to Peripheral Neuropathy

	Dose modification of Oxaliplatin (mg/m²/cycle)		
	Duration of Peripheral Neuropathy		
Type of Toxicity	≤ 7 days	Non persistent > 7 and < 14 days	Persistent between courses
Cold-related dysaesthesia	None	None	None
Paraesthesia	None	None	Stop until recovery, then restart at 75
Paraesthesia associated with pain or functional impairment	None	75	Stop treatment

If the dose of oxaliplatin must be reduced due to one or more of the toxicities listed in the above tables, then escalation of the dose back to the starting level is not permitted. However, temporary reductions in dose are permissible at investigator discretion for patients in the SIRT arm *if* dose reduction was made due to low white blood cell counts between cycles 2-5 possibly due to the myelosuppressive effect of SIRT.

Chronic neuropathy
Upon evidence of chronic neuropathy, treatment is to continue with 5-FU/LV alone until such time as any of the following conditions are met:

- Objective evidence of tumour progression at any site as determined by CT scan and/or X-ray and/or ultrasound and/or clinical examination.
- Patient's request.
- Complete radiological response to therapy.
- Unacceptable toxicity as determined by objective evidence, clinical judgement or patient request.

Oxaliplatin may be reintroduced to the treatment, subject to investigator discretion, at any time prior to objective evidence of disease progression.

The SIRFLOX/FF-Global Trial Protocols stated the following:
The toxicity of each cycle of chemotherapy must be recorded before the administration of the next one and graded according to the NCI Common Toxicity Criteria (NCI-CTC) version 3.0.

Dose modifications will be made according to the worst toxicity observed during the previous cycle. Treatment should be delayed until full recovery of stomatitis or diarrhoea, and recovery to ≤ NCI grade 2 skin or other toxicity. Blood counts should have recovered to:

Neutrophils > 1 x 10^9/L
Platelets > 75 x 10^9/L

The recommended initial dose modifications in the event of toxicity due to FOLFOX6m chemotherapy are detailed in the following tables. Subsequent dose modifications can be made by reducing the concentration of the active constituents by 25%. All treatment modifications should be documented on the chemotherapy and toxicity flow sheet.

Table: Recommended Dose Modification Due to FOLFOX6m Toxicity (excludes neurosensory toxicity)

Type of Toxicity (NCI-CTC Grade)	Initial Doses (mg/m^2/cycle)		
	5-FU IV bolus	5-FU IV continuous infusion	Oxaliplatin
	400	2400	85
	Dose modifications of study drugs (mg/m^2/cycle) (LV dose should not be modified)		
Hemoglobin (any grade)	none	none	none
White blood cells (any grade)	none	none	none
Neutrophils grade 3 or 4	300	1800	65
Platelets grade 3 or 4	300	1800	65
Nausea and/or vomiting grade 4 despite adequate anti-emetic treatment	Stop treatment.		
Diarrhoea grade 3	300	1800	none
Diarrhoea grade 4*	300	1800	65
Stomatitis grade 3	300	1800	none
Stomatitis grade 4*	300	1800	65
Heart ≥ grade 2	Stop treatment.		

Skin grade 3 or 4	300	1800	none
Allergy grade 3 or 4	Stop treatment.		
Neurocerebellar	Stop treatment.		
Neurosensory: specific adaptation according to symptomatology	none	none	As described in Table B
Alopecia (any grade)	none	none	none
Local intolerance (any grade)	none	none	none
Other toxicity clearly drug related:			
- grade 1 or 2	none	none	none
- grade 3	300	1800	65
- grade 4	Stop treatment	Stop treatment	Stop treatment

*or repeated grade 3 after 5-FU dose reduction

The oxaliplatin dose should be reduced in the next cycle according to the specific grade of peripheral neuropathy observed after a given cycle of chemotherapy (Table B).

Table: Recommended Dose Modification of Oxaliplatin Due to Peripheral Neuropathy

Dose modification of oxaliplatin (mg/m²/cycle)			
Type of Toxicity	Duration of Peripheral Neuropathy		
	≤ 7 days	Non persistent > 7 and < 14 days	Persistent between courses
Cold-related dysaesthesia	none	none	none
Paraesthesia	none	none	Stop until recovery, then restart at 75
Paraesthesia associated with pain or functional impairment	none	75	Stop treatment

If the dose of oxaliplatin must be reduced due to one or more of the toxicities listed in Tables A or B, above, then escalation of the dose back to the starting level is not permitted. However, temporary reductions in dose are permissible at investigator discretion for patients in the SIRT arm when toxicities are clearly attributable to the implantation of SIRT microspheres.

Modification of Infusion Duration of Oxaliplatin
In the case of Laryngeal Spasm Syndrome or in the case of NCI grade ≤ 2 allergy, increase the oxaliplatin infusion time from 2 to 6 hours.

Schedule Modifications
The dosage schedule should be followed. A delay of 7 days or less in the start date of cycles of chemotherapy is acceptable. If the start of a chemotherapy cycle has to be delayed for more than 3 consecutive weeks due to the same chemotherapy related toxicity, then treatment must be discontinued due to toxicity. The patient will continue to be followed as per protocol, including 8-weekly disease assessments.

Delays of longer than 3 weeks are permitted for non-chemotherapy related toxicities, adverse events or elective surgery. Chemotherapy must be recommenced at the earliest opportunity and continued as per protocol, including 8-weekly study assessments.

Frequency and type of laboratory monitoring

FOXFIRE Trial Protocol:

FBC & platelets*	Each week that chemotherapy is administered.
Bilirubin, ALT, AST, ALP, LDH, Urea, Creatinine, Protein, Albumin*	Each week that chemotherapy is administered. If abnormal at completion of protocol therapy, continue to check every 4 weeks until normal.
CEA	4 weekly while on chemotherapy then 8 weekly up to 18 months.

* These tests need only be performed while the patient is receiving chemotherapy

SIRFLOX/FF-Global Trial Protocols:

Haematological**	Prior to each cycle of chemotherapy administration or 8 *** weekly if the patient is off protocol chemotherapy.
Biochemistry**	Prior to each cycle of chemotherapy administration or 8 ***weekly if the patient is off protocol chemotherapy
CEA	4 weekly until progression.

** *These tests need only be performed while the patient is receiving chemotherapy.*
*** In case of > 12 months follow up after complete resection of disease or lasting CR (see above) the interval may be increased to 12 weeks coinciding with imaging visits.

Switching to other protocol therapies

FOXFIRE Trial:
In FOXFIRE, the protocol stated: If a patient requires removal of a long line due to infection or venous thrombosis or other complication, and should the treating oncologist wish to consider capecitabine therapy as an alternative to line re-insertion for infusional 5-FU, then the following conditions will apply:

- APPROVAL MUST BE OBTAINED from the FOXFIRE trial office before capecitabine is substituted for 5-FU, and investigators must follow the guidelines in Appendix 11 for the treatment schedule to be used.
- Capecitabine should be continued until the patient has completed 6 months of chemotherapy in total, which includes the protocol chemotherapy received before the capecitabine was started.
- For patients in Arm A of the trial, substitution of therapy can be performed at any time following a line complication. The FOXFIRE trial office must be informed immediately.
- For patients in Arm B of the trial, substitution of therapy can be performed only once the patient has reached cycle 6 of treatment. Prior to cycle 6, OxMdG must be continued as per protocol. The FOXFIRE trial office must be informed immediately.

SIRFLOX/FF-Global Trials:

In SIRFLOX and FOXFIRE-Global, no switching to other protocol therapy was permitted.

Supplementary Figures

Figure S1: Kaplan-Meier overall survival curves by treatment arm for FOXFIRE, SIRFLOX and FOXFIRE-Global

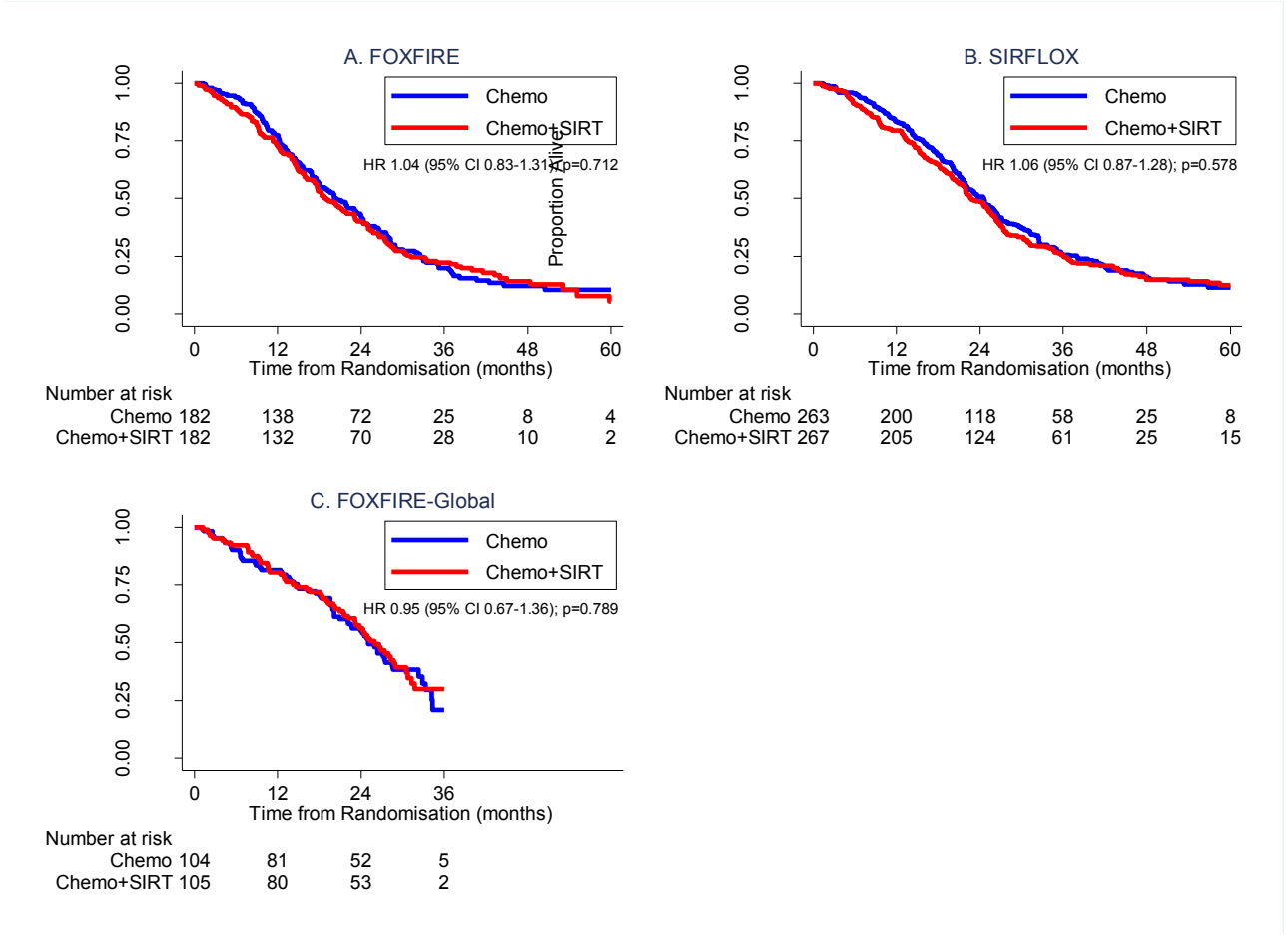


Figure S2: A. Waterfall plot of largest reduction in the sum of longest diameters of target lesions over the entire study duration by treatment arm, and B. Forest plot of response rate odds ratios

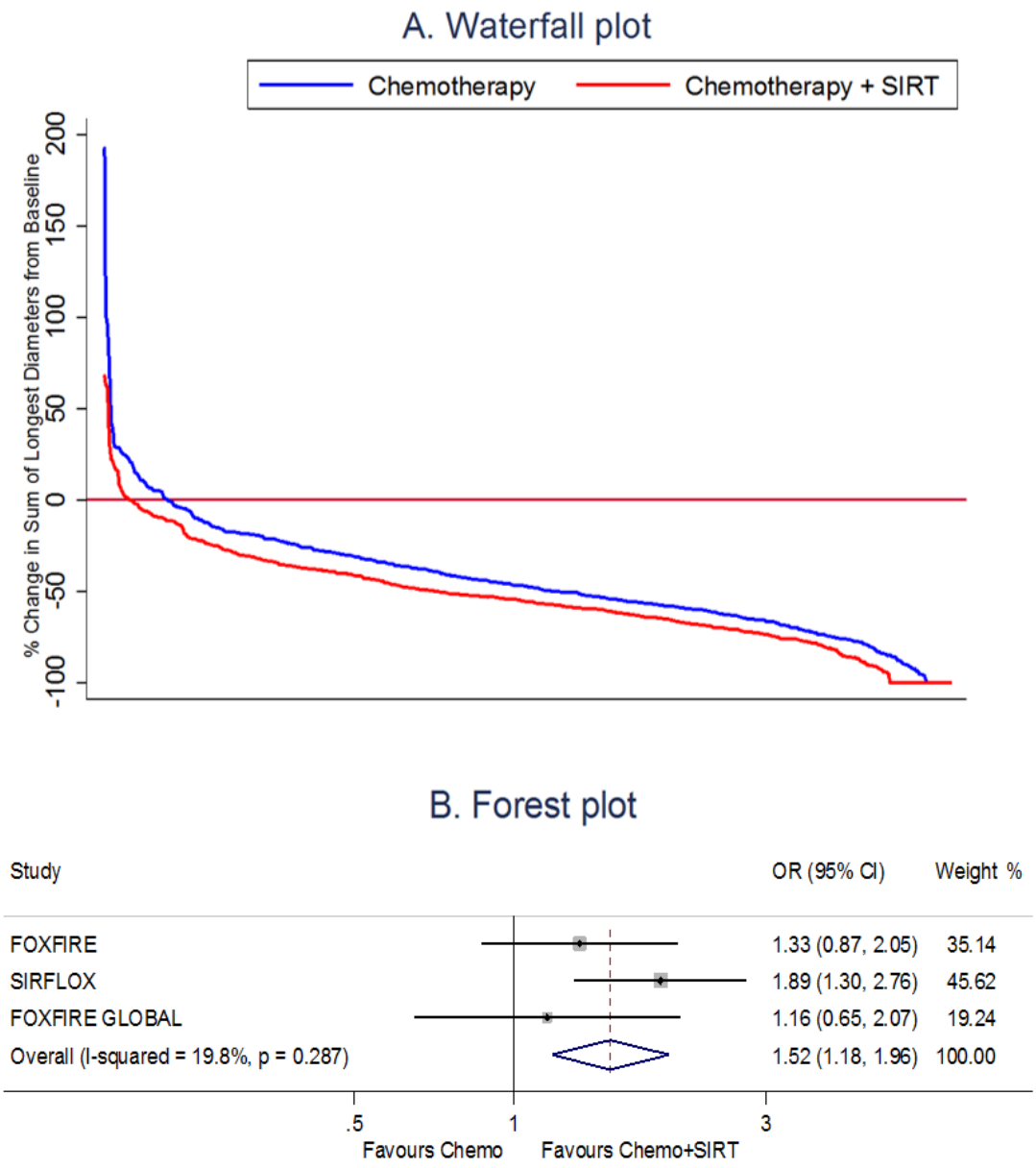


Figure S3: Odds ratios for undergoing a resection (n=1103)

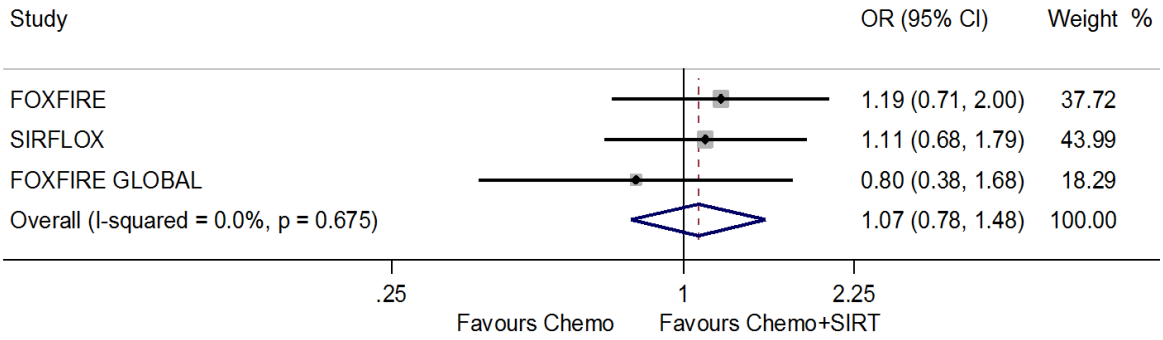


Figure S4: Percentage of patients with grade 3-5 AEs per cycle (n=1078)

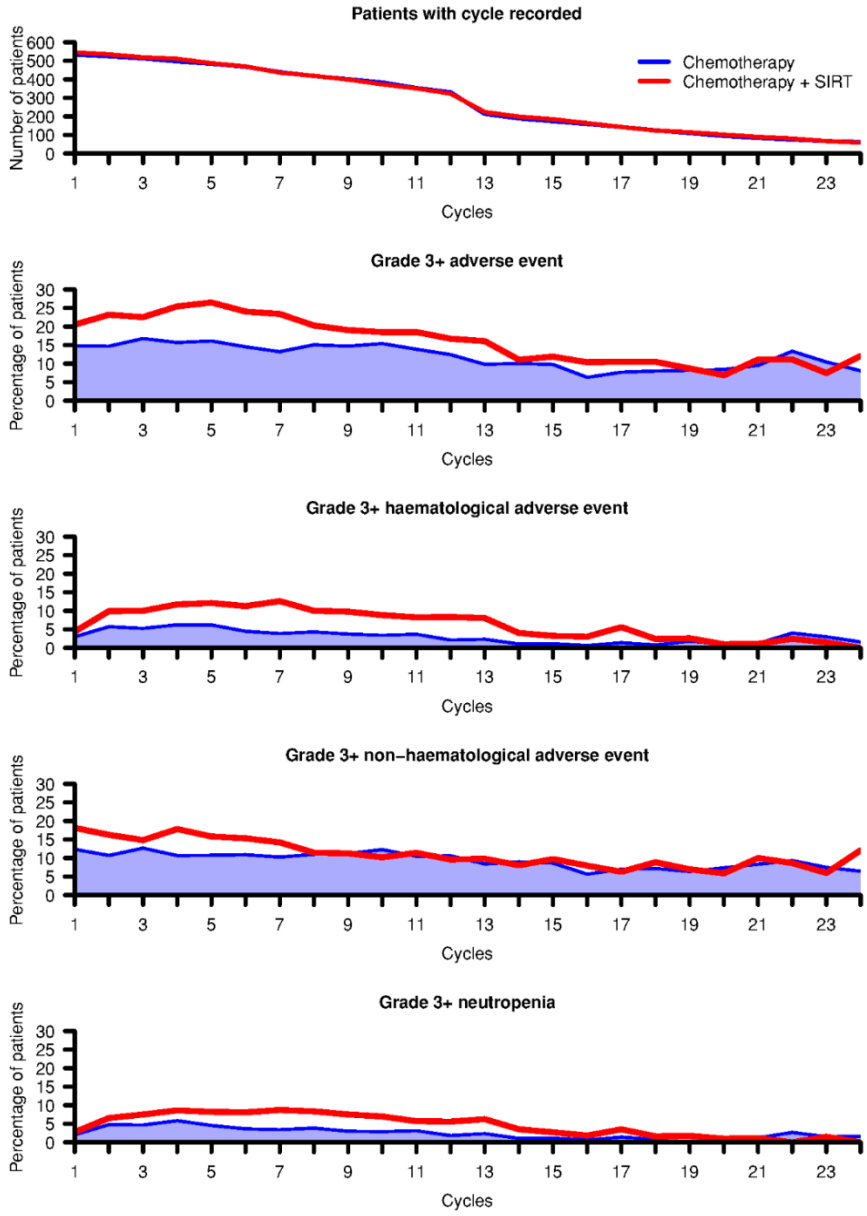
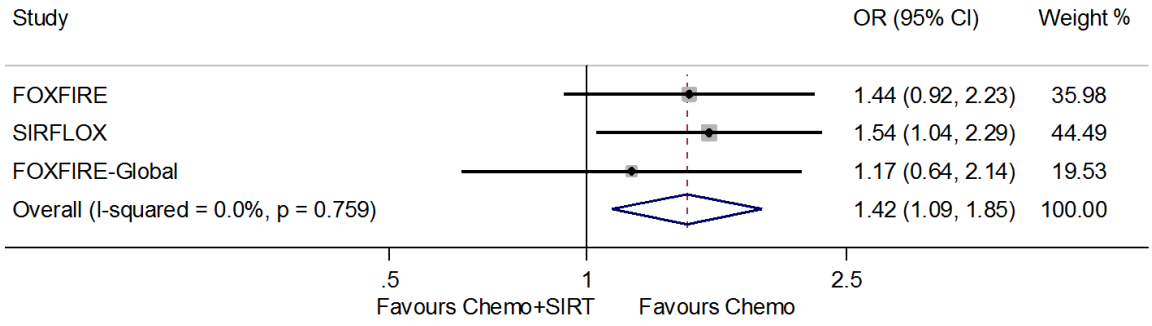


Figure S5: Odds ratios for experiencing a grade 3-5 adverse event (n=1078)



Supplementary Tables

Table S1. Recruitment dates, follow-up dates and objectives for the FOXFIRE, SIRFLOX and FOXFIRE-Global trials

	FOXFIRE	SIRFLOX	FOXFIRE-Global
Start of recruitment	13Nov2009	11Oct2006	20May2013
End of recruitment	31Oct2014	25Apr2013	23Dec2014
End of follow-up	31Oct2016	01Jun2016	30Nov2016
Number of recruiting centres	25	87	67
Primary objective	Overall survival	Progression-free survival	Overall survival
Secondary objectives	Progression-free survival	Overall survival	Progression-free survival
	Progression-free survival in the liver	Progression-free survival in the liver	Progression-free survival in the liver
	Toxicity and safety	Toxicity and safety	Toxicity and safety
	Tumour response rate	Tumour response rate	Tumour response rate
	Quality of Life	Quality of Life	Quality of Life
	Liver resection rate	Liver resection rate	Liver resection rate
		Hepatic and extra-hepatic recurrence rate	Hepatic and extra-hepatic recurrence rate
	Health costs/economics		Health economics
	Proportion of patients receiving second line treatment		
	Time to second line treatment		

Table S2. Reasons for treatment discontinuation in FOXFIRE (n=364)

	FOXFIRE		
	Chemotherapy (n=182)	Chemotherapy + SIRT (n=182)	Overall (n=364)
Completed Study Treatment	**86 (47.3%)**	**77 (42.3%)**	**163 (44.8%)**
Treatment not Started	3 (1.6%)	2 (1.1%)	5 (1.4%)
Patient Decision	7 (3.8%)	10 (5.5%)	17 (4.7%)
Clinical Decision	25 (13.7%)	26 (14.3%)	51 (14.0%)
Disease Progression	28 (15.4%)	19 (10.4%)	47 (12.9%)
Adverse Event	6 (3.3%)	9 (4.9%)	15 (4.1%)
Serious Adverse Event	9 (4.9%)	16 (8.8%)	25 (6.9%)
Death	6 (3.3%)	9 (4.9%)	15 (4.1%)
Protocol Violation/Ineligibility		1 (0.5%)	1 (0.3%)
Other	5 (2.7%)	6 (3.3%)	11 (3.0%)
Unknown	7 (3.8%)	7 (3.8%)	14 (3.8%)

Table S3: Baseline characteristics of participants in the FOXFIRE (n=364), SIRFLOX (n=530) and FOXFIRE-Global (n=209) trials

		FOXFIRE			SIRFLOX			FOXFIRE GLOBAL		
		Chemotherapy (n=182)	Chemotherapy + SIRT (n=182)	Overall (n=364)	Chemotherapy (n=263)	Chemotherapy + SIRT (n=267)	Overall (n=530)	Chemotherapy (n=104)	Chemotherapy + SIRT (n=105)	Overall (n=209)
Age at randomisation (years)[1]		62.0 (30.0,84.0)	63.5 (30.0,83.0)	62.5 (30.0,84.0)	63.3 (23.1,89.0)	63.4 (28.4,80.8)	63.4 (23.1,89.0)	63.0 (37.6,82.3)	63.1 (29.2,89.6)	63.1 (29.2,89.6)
Time since diagnosis of primary tumor to randomisation (months)[2]		1.5 (1.0,2.6)	1.5 (1.1,2.7)	1.5 (1.0,2.7)	1.3 (0.7,2.3)	1.3 (0.8,2.1)	1.3 (0.8,2.2)	1.3 (0.8,2.0)	1.1 (0.7,2.0)	1.2 (0.7,2.0)
Time since diagnosis of liver metastases to randomisation (months)[2]		1.2 (0.9,1.9)	1.3 (0.9,1.9)	1.3 (0.9,1.9)	1.2 (0.7,1.8)	1.2 (0.7,1.8)	1.2 (0.7,1.8)	1.2 (0.7,1.7)	1.0 (0.6,1.7)	1.1 (0.7,1.7)
Gender	Male	127 (69.8%)	117 (64.3%)	244 (67.0%)	174 (66.2%)	182 (68.2%)	356 (67.2%)	60 (57.7%)	64 (61.0%)	124 (59.3%)
	Female	55 (30.2%)	65 (35.7%)	120 (33.0%)	88 (33.5%)	85 (31.8%)	173 (32.6%)	44 (42.3%)	41 (39.0%)	85 (40.7%)
	Missing				1 (0.4%)		1 (0.2%)			
WHO performance status	0	119 (65.4%)	117 (64.3%)	236 (64.8%)	175 (66.5%)	176 (65.9%)	351 (66.2%)	53 (51.0%)	61 (58.1%)	114 (54.5%)
	1	63 (34.6%)	64 (35.2%)	127 (34.9%)	87 (33.1%)	90 (33.7%)	177 (33.4%)	50 (48.1%)	44 (41.9%)	94 (45.0%)
	Missing		1 (0.5%)	1 (0.3%)	1 (0.4%)	1 (0.4%)	2 (0.4%)	1 (1.0%)		1 (0.5%)
Primary tumor site	Colon	127 (69.8%)	134 (73.6%)	261 (71.7%)	191 (72.6%)	215 (80.5%)	406 (76.6%)	74 (71.2%)	72 (68.6%)	146 (69.9%)
	Rectum	55 (30.2%)	48 (26.4%)	103 (28.3%)	60 (22.8%)	45 (16.9%)	105 (19.8%)	22 (21.2%)	23 (21.9%)	45 (21.5%)
	Not Categorisable[3]				5 (1.9%)	2 (0.7%)	7 (1.3%)	3 (2.9%)	3 (2.9%)	6 (2.9%)
	Missing				7 (2.7%)	5 (1.9%)	12 (2.3%)	5 (4.8%)	7 (6.7%)	12 (5.7%)
Primary tumor in situ?	Yes	122 (67.0%)	109 (59.9%)	231 (63.5%)	121 (46.0%)	119 (44.6%)	240 (45.3%)	59 (56.7%)	50 (47.6%)	109 (52.2%)
	No	60 (33.0%)	72 (39.6%)	132 (36.3%)	141 (53.6%)	148 (55.4%)	289 (54.5%)	45 (43.3%)	55 (52.4%)	100 (47.8%)
	Missing		1 (0.5%)	1 (0.3%)	1 (0.4%)		1 (0.2%)			
Prior adjuvant chemotherapy?	Yes	9 (4.9%)	14 (7.7%)	23 (6.3%)	16 (6.1%)	13 (4.9%)	29 (5.5%)	3 (2.9%)	4 (3.8%)	7 (3.3%)
	No	173 (95.1%)	168 (92.3%)	341 (93.7%)	246 (93.5%)	254 (95.1%)	500 (94.3%)	101 (97.1%)	101 (96.2%)	202 (96.7%)
	Missing				1 (0.4%)		1 (0.2%)			
Metastases present at initial diagnosis?	Yes - Synchronous	154 (84.6%)	150 (82.4%)	304 (83.5%)	227 (86.3%)	240 (89.9%)	467 (88.1%)	94 (90.4%)	93 (88.6%)	187 (89.5%)
	No - Metachronous	27 (14.8%)	30 (16.5%)	57 (15.7%)	34 (12.9%)	26 (9.7%)	60 (11.3%)	10 (9.6%)	12 (11.4%)	22 (10.5%)
	Missing	1 (0.5%)	2 (1.1%)	3 (0.8%)	2 (0.8%)	1 (0.4%)	3 (0.6%)			
Extra-hepatic metastases status[4]	No	122 (67.0%)	121 (66.5%)	243 (66.8%)	159 (60.5%)	161 (60.3%)	320 (60.4%)	77 (74.0%)	73 (69.5%)	150 (71.8%)
	Yes	60 (33.0%)	61 (33.5%)	121 (33.2%)	104 (39.5%)	106 (39.7%)	210 (39.6%)	27 (26.0%)	32 (30.5%)	59 (28.2%)
Extra-hepatic metastases sites	Lungs	26 (43.3%)	19 (31.1%)	45 (37.2%)	35 (33.7%)	40 (37.7%)	75 (35.7%)	11 (40.7%)	12 (37.5%)	23 (39.0%)
	Lungs & lymph nodes	4 (6.7%)	4 (6.6%)	8 (6.6%)	18 (17.3%)	14 (13.2%)	32 (15.2%)	1 (3.7%)	5 (15.6%)	6 (10.2%)
	Lungs & Other	1 (1.7%)		1 (0.8%)	1 (1.0%)		1 (0.5%)	1 (3.7%)		1 (1.7%)

		FOXFIRE			SIRFLOX			FOXFIRE GLOBAL		
		Chemotherapy (n=182)	Chemotherapy + SIRT (n=182)	Overall (n=364)	Chemotherapy (n=263)	Chemotherapy + SIRT (n=267)	Overall (n=530)	Chemotherapy (n=104)	Chemotherapy + SIRT (n=105)	Overall (n=209)
	Lymph nodes	18 (30.0%)	21 (34.4%)	39 (32.2%)	46 (44.2%)	45 (42.5%)	91 (43.3%)	14 (51.9%)	12 (37.5%)	26 (44.1%)
	Lymph nodes & Other	2 (3.3%)		2 (1.7%)	2 (1.9%)	2 (1.9%)	4 (1.9%)		1 (3.1%)	1 (1.7%)
	Other	5 (8.3%)	5 (8.2%)	10 (8.3%)		2 (1.9%)	2 (1.0%)		2 (6.2%)	2 (3.4%)
	Missing	4 (6.7%)	12 (19.7%)	16 (13.2%)	2 (1.9%)	3 (2.8%)	5 (2.4%)			
Degree of liver involvement[4]	<=25%	114 (62.6%)	115 (63.2%)	229 (62.9%)	192 (73.0%)	185 (69.3%)	377 (71.1%)	74 (71.2%)	74 (70.5%)	148 (70.8%)
	>25%	68 (37.4%)	67 (36.8%)	135 (37.1%)	70 (26.6%)	81 (30.3%)	151 (28.5%)	30 (28.8%)	31 (29.5%)	61 (29.2%)
	Missing				1 (0.4%)	1 (0.4%)	2 (0.4%)			
Treating region[5]	Australia				98 (37.3%)	93 (34.8%)	191 (36.0%)	42 (40.4%)	36 (34.3%)	78 (37.3%)
	Belgium				7 (2.7%)	21 (7.9%)	28 (5.3%)	4 (3.8%)	5 (4.8%)	9 (4.3%)
	France				14 (5.3%)	14 (5.2%)	28 (5.3%)	15 (14.4%)	12 (11.4%)	27 (12.9%)
	Germany				48 (18.3%)	33 (12.4%)	81 (15.3%)	3 (2.9%)	3 (2.9%)	6 (2.9%)
	Israel				14 (5.3%)	22 (8.2%)	36 (6.8%)	6 (5.8%)	11 (10.5%)	17 (8.1%)
	Italy				1 (0.4%)	1 (0.4%)	2 (0.4%)	3 (2.9%)	7 (6.7%)	10 (4.8%)
	Korea, Republic Of							2 (1.9%)	3 (2.9%)	5 (2.4%)
	New Zealand				43 (16.3%)	45 (16.9%)	88 (16.6%)	10 (9.6%)	4 (3.8%)	14 (6.7%)
	Portugal							2 (1.9%)		2 (1.0%)
	Singapore							1 (1.0%)		1 (0.5%)
	Spain				8 (3.0%)	9 (3.4%)	17 (3.2%)	6 (5.8%)	4 (3.8%)	10 (4.8%)
	Taiwan, Province Of China							3 (2.9%)	4 (3.8%)	7 (3.3%)
	United Kingdom	182 (100.0%)	182 (100.0%)	364 (100.0%)						
	United States				30 (11.4%)	29 (10.9%)	59 (11.1%)	7 (6.7%)	16 (15.2%)	23 (11.0%)
Intention to treat with biological agents[4]	Yes	65 (35.7%)	65 (35.7%)	130 (35.7%)	147 (55.9%)	146 (54.7%)	293 (55.3%)	87 (83.7%)	87 (82.9%)	174 (83.3%)
	No	96 (52.7%)	95 (52.2%)	191 (52.5%)	40 (15.2%)	40 (15.0%)	80 (15.1%)	17 (16.3%)	18 (17.1%)	35 (16.7%)
	Not applicable[6]	21 (11.5%)	22 (12.1%)	43 (11.8%)	76 (28.9%)	81 (30.3%)	157 (29.6%)			

[1] Mean (standard deviation)
[2] Median (interquartile range)
[3] Patient's site of primary tumour recorded as being both colon and rectum. Note: only options for FOXFIRE were colon or rectum
[4] Minimisation factors
[5] The minimisation factor was centre, not treating region (28, 87 and 69 centres in total in FOXFIRE, SIRFLOX & FOXFIRE-Global, respectively)
[6] Intention to treat with a biological agent was not a minimisation variable for these patients as it was introduced after these patients entered the study

Table S4: Treatment exposure subsequent to trial-specified treatment (n=1103)

	FOXFIRE			SIRFLOX			FOXFIRE GLOBAL			COMBINED			
	Chemotherapy (n=182)	Chemotherapy + SIRT (n=182)	Overall (n=364)	Chemotherapy (n=263)	Chemotherapy + SIRT (n=267)	Overall (n=530)	Chemotherapy (n=104)	Chemotherapy + SIRT (n=105)	Overall (n=209)	Chemotherapy (n=549)	Chemotherapy + SIRT (n=554)	Overall (n=1103)	Mantel-Haenszel statistic; P-Value[1]
Subsequent Chemo	136 (74.7%)	121 (66.5%)	257 (70.6%)	196 (74.5%)	197 (73.8%)	393 (74.2%)	74 (71.2%)	58 (55.2%)	132 (63.2%)	406 (74.0%)	376 (67.9%)	782 (70.9%)	**4.99; 0.026**[2]
Oxaliplatin	46 (25.3%)	46 (25.3%)	92 (25.3%)	73 (27.8%)	70 (26.2%)	143 (27.0%)	25 (24.0%)	21 (20.0%)	46 (22.0%)	144 (26.2%)	137 (24.7%)	281 (25.5%)	
Oxaliplatin Continued	12 (6.6%)	10 (5.5%)	22 (6.0%)	26 (9.9%)	23 (8.6%)	49 (9.2%)	5 (4.8%)	8 (7.6%)	13 (6.2%)	43 (7.8%)	41 (7.4%)	84 (7.6%)	0.08; 0.782
Fluorouracil	102 (56.0%)	85 (46.7%)	187 (51.4%)	168 (63.9%)	164 (61.4%)	332 (62.6%)	67 (64.4%)	50 (47.6%)	117 (56.0%)	337 (61.4%)	299 (54.0%)	636 (57.7%)	6.31; 0.012[2]
Irinotecan	122 (67.0%)	103 (56.6%)	225 (61.8%)	181 (68.8%)	171 (64.0%)	352 (66.4%)	63 (60.6%)	42 (40.0%)	105 (50.2%)	366 (66.7%)	316 (57.0%)	682 (61.8%)	10.99; 0.001[2]
Anti-EGFR	31 (17.0%)	33 (18.1%)	64 (17.6%)	79 (30.0%)	61 (22.8%)	140 (26.4%)	31 (29.8%)	14 (13.3%)	45 (21.5%)	141 (25.7%)	108 (19.5%)	249 (22.6%)	6.13; 0.013[2]
Anti-VEGF	55 (30.2%)	44 (24.2%)	99 (27.2%)	90 (34.2%)	75 (28.1%)	165 (31.1%)	41 (39.4%)	30 (28.6%)	71 (34.0%)	186 (33.9%)	149 (26.9%)	335 (30.4%)	6.38; 0.012[2]
Regorafenib	1 (0.6%)		1 (0.3%)	14 (5.3%)	22 (8.2%)	36 (6.8%)	5 (4.8%)	4 (3.8%)	9 (4.3%)	20 (3.6%)	26 (4.7%)	46 (4.2%)	
Mitomycin C	7 (3.8%)	3 (1.6%)	10 (2.7%)	19 (7.2%)	11 (4.1%)	30 (5.7%)	1 (1.0%)	3 (2.9%)	4 (1.9%)	27 (4.9%)	17 (3.1%)	44 (4.0%)	
Study – VEGF/placebo	3 (1.6%)	2 (1.1%)	5 (1.4%)	7 (2.7%)	3 (1.1%)	10 (1.9%)	2 (1.9%)	3 (2.9%)	5 (2.4%)	12 (2.2%)	8 (1.4%)	20 (1.8%)	
Study – EGFR/placebo				3 (1.1%)	1 (0.4%)	4 (0.8%)	1 (1.0%)		1 (0.5%)	4 (0.7%)	1 (0.2%)	5 (0.5%)	
Study – Other	3 (1.6%)	4 (2.2%)	7 (1.9%)	8 (3.0%)	6 (2.2%)	14 (2.6%)	1 (1.0%)		1 (0.5%)	12 (2.2%)	10 (1.8%)	22 (2.0%)	
Other Chemo	5 (2.7%)	2 (1.1%)	7 (1.9%)	6 (2.3%)	10 (3.7%)	16 (3.0%)	3 (2.9%)	4 (3.8%)	7 (3.3%)	14 (2.6%)	16 (2.9%)	30 (2.7%)	
Subsequent Non-Chemo	77 (42.3%)	71 (39.0%)	148 (40.7%)	123 (46.8%)	110 (41.2%)	233 (44.0%)	26 (25.0%)	29 (27.6%)	55 (26.3%)	226 (41.2%)	210 (37.9%)	436 (39.5%)	**1.25; 0.263**
Surgery – Liver	13 (7.1%)	25 (13.7%)	38 (10.4%)	10 (3.8%)	6 (2.2%)	16 (3.0%)	4 (3.8%)		4 (1.9%)	27 (4.9%)	31 (5.6%)	58 (5.3%)	
Surgery – Non Liver	21 (11.5%)	27 (14.8%)	48 (13.2%)	5 (1.9%)	7 (2.6%)	12 (2.3%)	1 (1.0%)	2 (1.9%)	3 (1.4%)	27 (4.9%)	36 (6.5%)	63 (5.7%)	
Ablation – Liver	4 (2.2%)	1 (0.5%)	5 (1.4%)	4 (1.5%)	5 (1.9%)	9 (1.7%)	1 (1.0%)		1 (0.5%)	9 (1.6%)	6 (1.1%)	15 (1.4%)	
Ablation – Non Liver	7 (3.8%)	12 (6.6%)	19 (5.2%)	2 (0.8%)	3 (1.1%)	5 (0.9%)		1 (1.0%)	1 (0.5%)	9 (1.6%)	16 (2.9%)	25 (2.3%)	
Radiotherapy – SIRT	20 (11.0%)	1 (0.5%)	21 (5.8%)	38 (14.4%)	11 (4.1%)	49 (9.2%)	8 (7.7%)	4 (3.8%)	12 (5.7%)	66 (12.0%)	16 (2.9%)	82 (7.4%)	
Radiotherapy – Non SIRT	29 (15.9%)	24 (13.2%)	53 (14.6%)	28 (10.6%)	35 (13.1%)	63 (11.9%)	6 (5.8%)	6 (5.7%)	12 (5.7%)	63 (11.5%)	65 (11.7%)	128 (11.6%)	
Chemoembolisation				5 (1.9%)	4 (1.5%)	9 (1.7%)	1 (1.0%)	2 (1.9%)	3 (1.4%)	6 (1.1%)	6 (1.1%)	12 (1.1%)	
Non Chemo – Other	13 (7.1%)	11 (6.0%)	24 (6.6%)	16 (6.1%)	12 (4.5%)	28 (5.3%)	4 (3.8%)	1 (1.0%)	5 (2.4%)	33 (6.0%)	24 (4.3%)	57 (5.2%)	

[1] Results from Mantel-Haenszel tests

[2] Statistically significantly different between treatment groups: $p < 0.05$

[3] Oxaliplatin is treated as "continued" if the patient received it within the first three months of ending trial protocol-specified treatment and had no other treatments in between

Table S5: Cause-specific and sub-distribution hazard ratios for liver-specific progression-free survival (n=1103)

Liver-Specific Progression-Free Survival		HR (95% CI)	
		Liver progression (n=444)	**Non-liver progression or death without progression (n=497)**
Treatment	Sub-distribution HR	0.51 (0.43 – 0.62)	1.76 (1.47 – 2.11)
	Cause-specific HR	0.57 (0.47 – 0.69)[1]	1.36 (1.13 – 1.62)[1]

[1] Time-constant estimates are provided: although there was a statistically significant departure from the proportional hazards assumption in both Cox models (p=0.018 and p=0.027 for liver and non-liver progression respectively), the residual plots did not indicate a major deviation from the proportional hazards assumption

Table S6: Best response (n=1103)

		Chemotherapy (n=549)	Chemotherapy + SIRT (n=554)	Overall (n=1103)
Objective response	Objective response (CR + PR)	345 (62.8%)	401 (72.4%)	746 (67.6%)
	Complete response (CR)	9 (1.6%)	25 (4.5%)	34 (3.1%)
	Partial response (PR)	336 (61.2%)	376 (67.9%)	712 (64.6%)
	Stable disease (SD)	142 (25.9%)	90 (16.3%)	232 (21.0%)
	Progressive Disease (PD)	23 (4.2%)	27 (4.9%)	50 (4.5%)
	Early death	14 (2.6%)	16 (2.9%)	30 (2.7%)
	Unknown	25 (4.6%)	20 (3.6%)	45 (4.1%)

Table S7: Best response achieved over the entire study period by individual trial

		FOXFIRE			SIRFLOX			FOXFIRE GLOBAL		
		Chemotherapy (n=182)	Chemotherapy + SIRT (n=182)	Overall (n=364)	Chemotherapy (n=263)	Chemotherapy + SIRT (n=267)	Overall (n=530)	Chemotherapy (n=104)	Chemotherapy + SIRT (n=105)	Overall (n=209)
Objective response (CR + PR)		111 (61.0%)	123 (67.6%)	234 (64.3%)	165 (62.7%)	205 (76.8%)	370 (69.8%)	69 (66.3%)	73 (69.5%)	142 (67.9%)
RECIST response	Complete response (CR)	4 (2.2%)	5 (2.7%)	9 (2.5%)	3 (1.1%)	15 (5.6%)	18 (3.4%)	2 (1.9%)	5 (4.8%)	7 (3.3%)
	Partial response (PR)	107 (58.8%)	118 (64.8%)	225 (61.8%)	162 (61.6%)	190 (71.2%)	352 (66.4%)	67 (64.4%)	68 (64.8%)	135 (64.6%)
	Stable disease (SD)	46 (25.3%)	27 (14.8%)	73 (20.1%)	71 (27.0%)	42 (15.7%)	113 (21.3%)	25 (24.0%)	21 (20.0%)	46 (22.0%)
	Progressive Disease (PD)	11 (6.0%)	11 (6.0%)	22 (6.0%)	7 (2.7%)	9 (3.4%)	16 (3.0%)	5 (4.8%)	7 (6.7%)	12 (5.7%)
	Early death	7 (3.8%)	9 (4.9%)	16 (4.4%)	3 (1.1%)	5 (1.9%)	8 (1.5%)	4 (3.8%)	2 (1.9%)	6 (2.9%)
	Unknown	7 (3.8%)	12 (6.6%)	19 (5.2%)	17 (6.5%)	6 (2.2%)	23 (4.3%)	1 (1.0%)	2 (1.9%)	3 (1.4%)

Table S8: Best liver-specific response achieved over the entire study period

		FOXFIRE			SIRFLOX			FOXFIRE GLOBAL		
		Chemotherapy (n=182)	Chemotherapy + SIRT (n=182)	Overall (n=364)	Chemotherapy (n=263)	Chemotherapy + SIRT (n=267)	Overall (n=530)	Chemotherapy (n=104)	Chemotherapy + SIRT (n=105)	Overall (n=209)
Objective response (CR + PR)		112 (61.5%)	128 (70.3%)	240 (65.9%)	167 (63.5%)	214 (80.2%)	381 (71.9%)	71 (68.3%)	78 (74.3%)	149 (71.3%)
RECIST response	Complete response (CR)	5 (2.8%)	5 (2.8%)	10 (2.8%)	3 (1.1%)	20 (7.5%)	23 (4.3%)	3 (2.9%)	8 (7.6%)	11 (5.3%)
	Partial response (PR)	107 (58.8%)	123 (67.6%)	230 (63.2%)	164 (62.4%)	194 (72.7%)	358 (67.6%)	68 (65.4%)	70 (66.7%)	138 (66.0%)
	Stable disease (SD)	45 (24.7%)	30 (16.5%)	75 (20.6%)	69 (26.2%)	36 (13.5%)	105 (19.8%)	24 (23.1%)	19 (18.1%)	43 (20.6%)
	Progressive Disease (PD)	11 (6.0%)	3 (1.6%)	14 (3.9%)	7 (2.7%)	6 (2.3%)	13 (2.5%)	4 (3.9%)	4 (3.8%)	8 (3.8%)
	Early death	7 (3.8%)	9 (4.9%)	16 (4.4%)	3 (1.1%)	5 (1.9%)	8 (1.5%)	4 (3.9%)	2 (1.9%)	6 (2.9%)
	Unknown	7 (3.8%)	12 (6.6%)	19 (5.2%)	17 (6.5%)	6 (2.3%)	23 (4.3%)	1 (1.0%)	2 (1.9%)	3 (1.4%)

Table S9: Worst reported adverse events (not cumulative) sorted by prevalence of patients with adverse events[1]

	Chemo alone				Chemo + SIRT			
Event Term	1 and 2	3	4	5	1 and 2	3	4	5
Neuropathy peripheral	307 (53.8%)	32 (5.6%)	1 (0.2%)	0 (0%)	273 (53.8%)	18 (3.6%)	0 (0%)	0 (0%)
Fatigue	275 (48.2%)	28 (4.9%)	0 (0%)	0 (0%)	261 (51.5%)	43 (8.5%)	0 (0%)	0 (0%)
Nausea	269 (47.1%)	6 (1.1%)	0 (0%)	0 (0%)	282 (55.6%)	13 (2.6%)	0 (0%)	0 (0%)
Diarrhoea	256 (44.8%)	35 (6.1%)	2 (0.4%)	0 (0%)	189 (37.3%)	33 (6.5%)	1 (0.2%)	0 (0%)
Neutropenia	50 (8.8%)	89 (15.6%)	48 (8.4%)	1 (0.2%)	55 (10.8%)	115 (22.7%)	71 (14.0%)	0 (0%)
Constipation	201 (35.2%)	5 (0.9%)	3 (0.5%)	0 (0%)	203 (40.0%)	8 (1.6%)	1 (0.2%)	0 (0%)
Decreased appetite	149 (26.1%)	5 (0.9%)	0 (0%)	0 (0%)	159 (31.4%)	8 (1.6%)	0 (0%)	0 (0%)
Vomiting	128 (22.4%)	8 (1.4%)	1 (0.2%)	0 (0%)	152 (30.0%)	20 (3.9%)	0 (0%)	0 (0%)
Abdominal pain	95 (16.6%)	13 (2.3%)	0 (0%)	0 (0%)	151 (29.8%)	30 (5.9%)	1 (0.2%)	0 (0%)
Thrombocytopenia	77 (13.5%)	6 (1.1%)	1 (0.2%)	0 (0%)	153 (30.2%)	37 (7.3%)	2 (0.4%)	0 (0%)
Mucosal inflammation	136 (23.8%)	9 (1.6%)	0 (0%)	0 (0%)	101 (19.9%)	6 (1.2%)	0 (0%)	0 (0%)
Dysgeusia	115 (20.1%)	1 (0.2%)	0 (0%)	0 (0%)	115 (22.7%)	0 (0%)	0 (0%)	0 (0%)
Epistaxis	122 (21.4%)	0 (0%)	0 (0%)	0 (0%)	102 (20.1%)	1 (0.2%)	0 (0%)	0 (0%)
Peripheral sensory neuropathy	110 (19.3%)	8 (1.4%)	0 (0%)	0 (0%)	89 (17.6%)	2 (0.4%)	0 (0%)	0 (0%)
Stomatitis	103 (18.0%)	6 (1.1%)	0 (0%)	0 (0%)	88 (17.4%)	6 (1.2%)	0 (0%)	0 (0%)
Alopecia	89 (15.6%)	1 (0.2%)	0 (0%)	0 (0%)	75 (14.8%)	0 (0%)	0 (0%)	0 (0%)
Pyrexia	70 (12.3%)	6 (1.1%)	0 (0%)	0 (0%)	73 (14.4%)	12 (2.4%)	1 (0.2%)	0 (0%)
Paraesthesia	77 (13.5%)	5 (0.9%)	0 (0%)	0 (0%)	58 (11.4%)	4 (0.8%)	0 (0%)	0 (0%)

	Chemo alone				Chemo + SIRT			
Event Term	1 and 2	3	4	5	1 and 2	3	4	5
Anaemia	57 (10.0%)	9 (1.6%)	3 (0.5%)	0 (0%)	56 (11.0%)	13 (2.6%)	0 (0%)	0 (0%)
Lethargy	66 (11.6%)	8 (1.4%)	0 (0%)	0 (0%)	52 (10.3%)	5 (1.0%)	0 (0%)	0 (0%)
Abdominal pain upper	28 (4.9%)	2 (0.4%)	1 (0.2%)	0 (0%)	90 (17.8%)	8 (1.6%)	0 (0%)	0 (0%)
Hypertension	60 (10.5%)	15 (2.6%)	0 (0%)	0 (0%)	43 (8.5%)	11 (2.2%)	0 (0%)	0 (0%)
Weight decreased	51 (8.9%)	0 (0%)	0 (0%)	0 (0%)	69 (13.6%)	9 (1.8%)	0 (0%)	0 (0%)
Rash	67 (11.7%)	1 (0.2%)	0 (0%)	0 (0%)	56 (11.0%)	0 (0%)	0 (0%)	0 (0%)
Insomnia	58 (10.2%)	0 (0%)	0 (0%)	0 (0%)	58 (11.4%)	1 (0.2%)	0 (0%)	0 (0%)
Palmar-plantar erythrodysaesthesia syndrome	69 (12.1%)	6 (1.1%)	0 (0%)	0 (0%)	36 (7.1%)	3 (0.6%)	0 (0%)	0 (0%)
Leukopenia	28 (4.9%)	10 (1.8%)	3 (0.5%)	0 (0%)	41 (8.1%)	20 (3.9%)	10 (2.0%)	0 (0%)
Pain	34 (6.0%)	5 (0.9%)	0 (0%)	0 (0%)	50 (9.9%)	17 (3.4%)	0 (0%)	0 (0%)
Headache	53 (9.3%)	2 (0.4%)	0 (0%)	0 (0%)	44 (8.7%)	3 (0.6%)	0 (0%)	0 (0%)
Cough	51 (8.9%)	1 (0.2%)	0 (0%)	0 (0%)	46 (9.1%)	0 (0%)	0 (0%)	0 (0%)
Asthenia	40 (7.0%)	5 (0.9%)	0 (0%)	0 (0%)	47 (9.3%)	3 (0.6%)	0 (0%)	0 (0%)
Dyspnoea	46 (8.1%)	2 (0.4%)	3 (0.5%)	0 (0%)	40 (7.9%)	2 (0.4%)	1 (0.2%)	1 (0.2%)
Back pain	33 (5.8%)	4 (0.7%)	1 (0.2%)	0 (0%)	48 (9.5%)	1 (0.2%)	0 (0%)	0 (0%)
Dizziness	47 (8.2%)	1 (0.2%)	0 (0%)	0 (0%)	35 (6.9%)	0 (0%)	0 (0%)	0 (0%)
Hypokalaemia	19 (3.3%)	7 (1.2%)	2 (0.4%)	0 (0%)	26 (5.1%)	12 (2.4%)	1 (0.2%)	0 (0%)
Gastrooesophageal reflux disease	42 (7.4%)	0 (0%)	0 (0%)	0 (0%)	23 (4.5%)	1 (0.2%)	0 (0%)	0 (0%)
Mouth ulceration	42 (7.4%)	2 (0.4%)	0 (0%)	0 (0%)	21 (4.1%)	0 (0%)	0 (0%)	0 (0%)
Oedema peripheral	18 (3.2%)	1 (0.2%)	0 (0%)	0 (0%)	43 (8.5%)	2 (0.4%)	0 (0%)	0 (0%)
Urinary tract infection	26 (4.6%)	3 (0.5%)	0 (0%)	0 (0%)	28 (5.5%)	2 (0.4%)	0 (0%)	0 (0%)
Chest pain	19 (3.3%)	3 (0.5%)	0 (0%)	0 (0%)	27 (5.3%)	9 (1.8%)	0 (0%)	0 (0%)
Pulmonary embolism	1 (0.2%)	7 (1.2%)	19 (3.3%)	0 (0%)	2 (0.4%)	4 (0.8%)	24 (4.7%)	0 (0%)
Rectal haemorrhage	27 (4.7%)	2 (0.4%)	0 (0%)	0 (0%)	23 (4.5%)	2 (0.4%)	0 (0%)	0 (0%)
Upper respiratory tract infection	28 (4.9%)	1 (0.2%)	0 (0%)	0 (0%)	21 (4.1%)	1 (0.2%)	0 (0%)	0 (0%)
Hiccups	22 (3.9%)	0 (0%)	0 (0%)	0 (0%)	26 (5.1%)	2 (0.4%)	0 (0%)	0 (0%)
Febrile neutropenia	0 (0%)	11 (1.9%)	5 (0.9%)	0 (0%)	0 (0%)	25 (4.9%)	7 (1.4%)	1 (0.2%)
Musculoskeletal pain	25 (4.4%)	1 (0.2%)	0 (0%)	0 (0%)	20 (3.9%)	2 (0.4%)	0 (0%)	0 (0%)
Dehydration	13 (2.3%)	5 (0.9%)	1 (0.2%)	0 (0%)	15 (3.0%)	10 (2.0%)	1 (0.2%)	0 (0%)
Abdominal distension	19 (3.3%)	0 (0%)	0 (0%)	0 (0%)	23 (4.5%)	2 (0.4%)	0 (0%)	0 (0%)
Pain in extremity	17 (3.0%)	4 (0.7%)	0 (0%)	0 (0%)	22 (4.3%)	0 (0%)	0 (0%)	0 (0%)
Procedural pain	6 (1.1%)	0 (0%)	0 (0%)	0 (0%)	31 (6.1%)	5 (1.0%)	0 (0%)	0 (0%)
Hyperglycaemia	7 (1.2%)	10 (1.8%)	5 (0.9%)	0 (0%)	12 (2.4%)	6 (1.2%)	1 (0.2%)	0 (0%)
Blood alkaline phosphatase increased	12 (2.1%)	1 (0.2%)	0 (0%)	0 (0%)	22 (4.3%)	2 (0.4%)	0 (0%)	0 (0%)
Hypotension	11 (1.9%)	4 (0.7%)	2 (0.4%)	0 (0%)	15 (3.0%)	4 (0.8%)	0 (0%)	0 (0%)
Ascites	2 (0.4%)	4 (0.7%)	0 (0%)	0 (0%)	23 (4.5%)	6 (1.2%)	0 (0%)	0 (0%)
Infection	5 (0.9%)	14 (2.5%)	0 (0%)	0 (0%)	11 (2.2%)	5 (1.0%)	0 (0%)	0 (0%)
Neurotoxicity	19 (3.3%)	1 (0.2%)	0 (0%)	0 (0%)	15 (3.0%)	0 (0%)	0 (0%)	0 (0%)
Lower respiratory tract infection	10 (1.8%)	5 (0.9%)	0 (0%)	0 (0%)	16 (3.2%)	3 (0.6%)	0 (0%)	0 (0%)
Lymphopenia	5 (0.9%)	1 (0.2%)	0 (0%)	0 (0%)	8 (1.6%)	16 (3.2%)	3 (0.6%)	0 (0%)
Pruritus	19 (3.3%)	0 (0%)	0 (0%)	0 (0%)	13 (2.6%)	1 (0.2%)	0 (0%)	0 (0%)
Aspartate aminotransferase increased	8 (1.4%)	2 (0.4%)	0 (0%)	0 (0%)	18 (3.6%)	4 (0.8%)	0 (0%)	0 (0%)
Polyneuropathy	17 (3.0%)	1 (0.2%)	0 (0%)	0 (0%)	11 (2.2%)	2 (0.4%)	0 (0%)	0 (0%)
Deep vein thrombosis	3 (0.5%)	7 (1.2%)	0 (0%)	0 (0%)	6 (1.2%)	10 (2.0%)	2 (0.4%)	0 (0%)
Hypomagnesaemia	19 (3.3%)	0 (0%)	0 (0%)	0 (0%)	7 (1.4%)	1 (0.2%)	0 (0%)	0 (0%)
Depression	8 (1.4%)	2 (0.4%)	0 (0%)	0 (0%)	15 (3.0%)	1 (0.2%)	0 (0%)	0 (0%)

	Chemo alone				Chemo + SIRT			
Event Term	1 and 2	3	4	5	1 and 2	3	4	5
Hypoalbuminaemia	5 (0.9%)	1 (0.2%)	0 (0%)	0 (0%)	14 (2.8%)	3 (0.6%)	0 (0%)	0 (0%)
Tremor	12 (2.1%)	1 (0.2%)	0 (0%)	0 (0%)	10 (2.0%)	0 (0%)	0 (0%)	0 (0%)
Alanine aminotransferase increased	4 (0.7%)	2 (0.4%)	0 (0%)	0 (0%)	14 (2.8%)	2 (0.4%)	0 (0%)	0 (0%)
Oral pain	12 (2.1%)	1 (0.2%)	0 (0%)	0 (0%)	9 (1.8%)	0 (0%)	0 (0%)	0 (0%)
Proctalgia	10 (1.8%)	0 (0%)	0 (0%)	0 (0%)	11 (2.2%)	1 (0.2%)	0 (0%)	0 (0%)
Chills	8 (1.4%)	0 (0%)	0 (0%)	0 (0%)	12 (2.4%)	1 (0.2%)	0 (0%)	0 (0%)
Confusional state	6 (1.1%)	5 (0.9%)	0 (0%)	0 (0%)	8 (1.6%)	2 (0.4%)	0 (0%)	0 (0%)
Intestinal obstruction	0 (0%)	10 (1.8%)	2 (0.4%)	0 (0%)	3 (0.6%)	5 (1.0%)	1 (0.2%)	0 (0%)
Neutropenic sepsis	2 (0.4%)	1 (0.2%)	4 (0.7%)	1 (0.2%)	0 (0%)	5 (1.0%)	7 (1.4%)	0 (0%)
Device related infection	8 (1.4%)	3 (0.5%)	0 (0%)	0 (0%)	3 (0.6%)	5 (1.0%)	0 (0%)	0 (0%)
Muscular weakness	9 (1.6%)	1 (0.2%)	0 (0%)	0 (0%)	8 (1.6%)	0 (0%)	0 (0%)	0 (0%)
Drug hypersensitivity	4 (0.7%)	1 (0.2%)	1 (0.2%)	0 (0%)	7 (1.4%)	4 (0.8%)	0 (0%)	0 (0%)
Hepatic pain	3 (0.5%)	1 (0.2%)	0 (0%)	0 (0%)	12 (2.4%)	1 (0.2%)	0 (0%)	0 (0%)
Hyponatraemia	5 (0.9%)	1 (0.2%)	0 (0%)	0 (0%)	4 (0.8%)	6 (1.2%)	1 (0.2%)	0 (0%)
Productive cough	9 (1.6%)	0 (0%)	0 (0%)	0 (0%)	7 (1.4%)	1 (0.2%)	0 (0%)	0 (0%)
Tachycardia	4 (0.7%)	2 (0.4%)	0 (0%)	0 (0%)	11 (2.2%)	0 (0%)	0 (0%)	0 (0%)
Syncope	0 (0%)	8 (1.4%)	1 (0.2%)	0 (0%)	1 (0.2%)	6 (1.2%)	0 (0%)	0 (0%)
Pneumonia	2 (0.4%)	3 (0.5%)	1 (0.2%)	0 (0%)	2 (0.4%)	6 (1.2%)	0 (0%)	1 (0.2%)
Thrombosis	4 (0.7%)	4 (0.7%)	0 (0%)	0 (0%)	3 (0.6%)	3 (0.6%)	1 (0.2%)	0 (0%)
Blood bilirubin increased	3 (0.5%)	2 (0.4%)	0 (0%)	0 (0%)	6 (1.2%)	3 (0.6%)	0 (0%)	0 (0%)
Fall	7 (1.2%)	0 (0%)	0 (0%)	0 (0%)	5 (1.0%)	2 (0.4%)	0 (0%)	0 (0%)
Hypersensitivity	9 (1.6%)	1 (0.2%)	0 (0%)	0 (0%)	1 (0.2%)	2 (0.4%)	0 (0%)	0 (0%)
Hypocalcaemia	4 (0.7%)	1 (0.2%)	0 (0%)	0 (0%)	8 (1.6%)	0 (0%)	0 (0%)	0 (0%)
Hypophosphataemia	1 (0.2%)	3 (0.5%)	0 (0%)	0 (0%)	6 (1.2%)	2 (0.4%)	1 (0.2%)	0 (0%)
Peripheral motor neuropathy	5 (0.9%)	1 (0.2%)	0 (0%)	0 (0%)	7 (1.4%)	0 (0%)	0 (0%)	0 (0%)
Blood albumin decreased	2 (0.4%)	0 (0%)	0 (0%)	0 (0%)	8 (1.6%)	1 (0.2%)	1 (0.2%)	0 (0%)
Blood potassium decreased	2 (0.4%)	2 (0.4%)	0 (0%)	0 (0%)	4 (0.8%)	4 (0.8%)	0 (0%)	0 (0%)
Dysphagia	6 (1.1%)	1 (0.2%)	0 (0%)	0 (0%)	5 (1.0%)	0 (0%)	0 (0%)	0 (0%)
Gastric ulcer	0 (0%)	0 (0%)	0 (0%)	0 (0%)	8 (1.6%)	3 (0.6%)	1 (0.2%)	0 (0%)
Neutrophil count	3 (0.5%)	2 (0.4%)	0 (0%)	0 (0%)	2 (0.4%)	3 (0.6%)	2 (0.4%)	0 (0%)
Blood creatinine increased	5 (0.9%)	1 (0.2%)	0 (0%)	0 (0%)	4 (0.8%)	1 (0.2%)	0 (0%)	0 (0%)
Dysaesthesia pharynx	5 (0.9%)	1 (0.2%)	0 (0%)	0 (0%)	5 (1.0%)	0 (0%)	0 (0%)	0 (0%)
Gout	5 (0.9%)	0 (0%)	0 (0%)	0 (0%)	5 (1.0%)	1 (0.2%)	0 (0%)	0 (0%)
Influenza	5 (0.9%)	1 (0.2%)	0 (0%)	0 (0%)	5 (1.0%)	0 (0%)	0 (0%)	0 (0%)
Intestinal perforation	0 (0%)	6 (1.1%)	2 (0.4%)	0 (0%)	0 (0%)	1 (0.2%)	1 (0.2%)	1 (0.2%)
Sepsis	1 (0.2%)	5 (0.9%)	2 (0.4%)	0 (0%)	0 (0%)	2 (0.4%)	1 (0.2%)	0 (0%)
Gastroenteritis	2 (0.4%)	0 (0%)	0 (0%)	0 (0%)	4 (0.8%)	4 (0.8%)	0 (0%)	0 (0%)
Infusion site infection	3 (0.5%)	2 (0.4%)	1 (0.2%)	0 (0%)	3 (0.6%)	1 (0.2%)	0 (0%)	0 (0%)
Orthostatic hypotension	5 (0.9%)	2 (0.4%)	0 (0%)	0 (0%)	3 (0.6%)	0 (0%)	0 (0%)	0 (0%)
Renal failure acute	3 (0.5%)	4 (0.7%)	0 (0%)	0 (0%)	1 (0.2%)	2 (0.4%)	0 (0%)	0 (0%)
C-reactive protein increased	4 (0.7%)	0 (0%)	0 (0%)	0 (0%)	3 (0.6%)	2 (0.4%)	0 (0%)	0 (0%)
Documented hypersensitivity to administered drug	4 (0.7%)	2 (0.4%)	0 (0%)	0 (0%)	2 (0.4%)	1 (0.2%)	0 (0%)	0 (0%)
Herpes zoster	6 (1.1%)	1 (0.2%)	0 (0%)	0 (0%)	2 (0.4%)	0 (0%)	0 (0%)	0 (0%)
Tooth abscess	4 (0.7%)	1 (0.2%)	0 (0%)	0 (0%)	4 (0.8%)	0 (0%)	0 (0%)	0 (0%)
Balance disorder	5 (0.9%)	0 (0%)	0 (0%)	0 (0%)	2 (0.4%)	1 (0.2%)	0 (0%)	0 (0%)
Duodenal ulcer	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	4 (0.8%)	3 (0.6%)	0 (0%)	0 (0%)
General physical health deterioration	3 (0.5%)	2 (0.4%)	0 (0%)	0 (0%)	0 (0%)	2 (0.4%)	0 (0%)	1 (0.2%)

	Chemo alone				Chemo + SIRT			
Event Term	1 and 2	3	4	5	1 and 2	3	4	5
Large intestinal obstruction	0 (0%)	5 (0.9%)	1 (0.2%)	0 (0%)	0 (0%)	1 (0.2%)	1 (0.2%)	0 (0%)
Malaise	3 (0.5%)	1 (0.2%)	0 (0%)	0 (0%)	3 (0.6%)	0 (0%)	1 (0.2%)	0 (0%)
Presyncope	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	4 (0.8%)	3 (0.6%)	0 (0%)	0 (0%)
Respiratory tract infection	5 (0.9%)	0 (0%)	0 (0%)	1 (0.2%)	2 (0.4%)	0 (0%)	0 (0%)	0 (0%)
Urinary retention	3 (0.5%)	0 (0%)	0 (0%)	0 (0%)	3 (0.6%)	2 (0.4%)	0 (0%)	0 (0%)
Visual impairment	4 (0.7%)	0 (0%)	0 (0%)	0 (0%)	3 (0.6%)	1 (0.2%)	0 (0%)	0 (0%)
Acute myocardial infarction	0 (0%)	0 (0%)	2 (0.4%)	1 (0.2%)	0 (0%)	2 (0.4%)	2 (0.4%)	0 (0%)
Anal fissure	3 (0.5%)	1 (0.2%)	0 (0%)	0 (0%)	3 (0.6%)	0 (0%)	0 (0%)	0 (0%)
Angina pectoris	2 (0.4%)	2 (0.4%)	0 (0%)	0 (0%)	2 (0.4%)	1 (0.2%)	0 (0%)	0 (0%)
Artery dissection	0 (0%)	0 (0%)	0 (0%)	0 (0%)	6 (1.2%)	1 (0.2%)	0 (0%)	0 (0%)
Diabetes mellitus	3 (0.5%)	0 (0%)	1 (0.2%)	0 (0%)	1 (0.2%)	1 (0.2%)	1 (0.2%)	0 (0%)
Frequent bowel movements	3 (0.5%)	0 (0%)	0 (0%)	0 (0%)	3 (0.6%)	1 (0.2%)	0 (0%)	0 (0%)
Gamma-glutamyltransferase increased	1 (0.2%)	1 (0.2%)	0 (0%)	0 (0%)	2 (0.4%)	3 (0.6%)	0 (0%)	0 (0%)
Gastrointestinal stoma complication	4 (0.7%)	0 (0%)	1 (0.2%)	0 (0%)	2 (0.4%)	0 (0%)	0 (0%)	0 (0%)
Groin pain	2 (0.4%)	1 (0.2%)	0 (0%)	0 (0%)	4 (0.8%)	0 (0%)	0 (0%)	0 (0%)
Hyperbilirubinaemia	1 (0.2%)	1 (0.2%)	0 (0%)	0 (0%)	2 (0.4%)	3 (0.6%)	0 (0%)	0 (0%)
Hypercalcaemia	3 (0.5%)	1 (0.2%)	0 (0%)	0 (0%)	2 (0.4%)	0 (0%)	1 (0.2%)	0 (0%)
Thrombosis in device	2 (0.4%)	1 (0.2%)	0 (0%)	0 (0%)	3 (0.6%)	1 (0.2%)	0 (0%)	0 (0%)
Asthma	2 (0.4%)	1 (0.2%)	0 (0%)	0 (0%)	2 (0.4%)	1 (0.2%)	0 (0%)	0 (0%)
Gastrointestinal haemorrhage	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	2 (0.4%)	1 (0.2%)	2 (0.4%)	0 (0%)
Hypoglycaemia	1 (0.2%)	1 (0.2%)	0 (0%)	0 (0%)	3 (0.6%)	0 (0%)	1 (0.2%)	0 (0%)
Infusion related reaction	1 (0.2%)	1 (0.2%)	0 (0%)	0 (0%)	4 (0.8%)	0 (0%)	0 (0%)	0 (0%)
Infusion site pain	2 (0.4%)	1 (0.2%)	0 (0%)	0 (0%)	3 (0.6%)	0 (0%)	0 (0%)	0 (0%)
Liver function test abnormal	0 (0%)	2 (0.4%)	0 (0%)	0 (0%)	2 (0.4%)	2 (0.4%)	0 (0%)	0 (0%)
Medical device complication	2 (0.4%)	1 (0.2%)	0 (0%)	0 (0%)	3 (0.6%)	0 (0%)	0 (0%)	0 (0%)
Radiation hepatitis	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (0.4%)	2 (0.4%)	0 (0%)	2 (0.4%)
Wound infection	3 (0.5%)	0 (0%)	0 (0%)	0 (0%)	2 (0.4%)	1 (0.2%)	0 (0%)	0 (0%)
Arteriospasm coronary	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	1 (0.2%)	2 (0.4%)	1 (0.2%)	0 (0%)
Device dislocation	2 (0.4%)	1 (0.2%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	1 (0.2%)	0 (0%)
Duodenitis	0 (0%)	0 (0%)	0 (0%)	0 (0%)	4 (0.8%)	1 (0.2%)	0 (0%)	0 (0%)
Embolism	1 (0.2%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	2 (0.4%)	1 (0.2%)	0 (0%)
Neutropenic infection	1 (0.2%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	3 (0.6%)	0 (0%)	0 (0%)
Pancytopenia	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	1 (0.2%)	1 (0.2%)	2 (0.4%)	0 (0%)
Phlebitis	2 (0.4%)	1 (0.2%)	0 (0%)	0 (0%)	2 (0.4%)	0 (0%)	0 (0%)	0 (0%)
Tooth extraction	4 (0.7%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Administration related reaction	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	2 (0.4%)	0 (0%)	0 (0%)
Anal abscess	1 (0.2%)	1 (0.2%)	0 (0%)	0 (0%)	1 (0.2%)	1 (0.2%)	0 (0%)	0 (0%)
Arterial spasm	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	2 (0.4%)	1 (0.2%)	0 (0%)	0 (0%)
Atrial fibrillation	0 (0%)	0 (0%)	0 (0%)	0 (0%)	3 (0.6%)	1 (0.2%)	0 (0%)	0 (0%)
Blood glucose increased	0 (0%)	2 (0.4%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	1 (0.2%)	0 (0%)
Blood phosphorus decreased	1 (0.2%)	2 (0.4%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Blood urea increased	2 (0.4%)	1 (0.2%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)
Cardiac failure	1 (0.2%)	1 (0.2%)	0 (0%)	0 (0%)	1 (0.2%)	1 (0.2%)	0 (0%)	0 (0%)
Cellulitis	2 (0.4%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)

	Chemo alone				Chemo + SIRT			
Event Term	1 and 2	3	4	5	1 and 2	3	4	5
Cholangitis	1 (0.2%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	2 (0.4%)	0 (0%)	0 (0%)
Decubitus ulcer	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	2 (0.4%)	1 (0.2%)	0 (0%)	0 (0%)
Delirium	1 (0.2%)	2 (0.4%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)
Device occlusion	1 (0.2%)	2 (0.4%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)
Incisional hernia	2 (0.4%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	1 (0.2%)	0 (0%)	0 (0%)
International normalised ratio increased	1 (0.2%)	1 (0.2%)	0 (0%)	0 (0%)	1 (0.2%)	1 (0.2%)	0 (0%)	0 (0%)
Large intestine perforation	0 (0%)	2 (0.4%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)
Leukocytosis	1 (0.2%)	2 (0.4%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)
Myocardial infarction	0 (0%)	1 (0.2%)	1 (0.2%)	0 (0%)	0 (0%)	1 (0.2%)	1 (0.2%)	0 (0%)
Myocardial ischaemia	1 (0.2%)	1 (0.2%)	0 (0%)	0 (0%)	1 (0.2%)	1 (0.2%)	0 (0%)	0 (0%)
Oesophageal candidiasis	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	2 (0.4%)	1 (0.2%)	0 (0%)	0 (0%)
Portal vein thrombosis	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	2 (0.4%)	0 (0%)	0 (0%)	1 (0.2%)
Post embolisation syndrome	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	2 (0.4%)	0 (0%)	0 (0%)
Renal failure	3 (0.5%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Somnolence	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	2 (0.4%)	1 (0.2%)	0 (0%)	0 (0%)
White blood cell count	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (0.4%)	1 (0.2%)	1 (0.2%)	0 (0%)
Acidosis	1 (0.2%)	0 (0%)	1 (0.2%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)
Adverse drug reaction	1 (0.2%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Cachexia	1 (0.2%)	1 (0.2%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)
Campylobacter gastroenteritis	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	1 (0.2%)	1 (0.2%)	0 (0%)	0 (0%)
Chronic obstructive pulmonary disease	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	1 (0.2%)
Hepatic function abnormal	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (0.4%)	0 (0%)	0 (0%)
Hernia	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (0.4%)	1 (0.2%)	0 (0%)	0 (0%)
Hyperkalaemia	1 (0.2%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)
Hypermagnesaemia	1 (0.2%)	1 (0.2%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)
Ileus	0 (0%)	3 (0.5%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Joint injury	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	1 (0.2%)	0 (0%)	0 (0%)
Jugular vein thrombosis	1 (0.2%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Lung infection	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	1 (0.2%)	0 (0%)
Pancreatitis	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	2 (0.4%)	0 (0%)	0 (0%)
Toxicity to various agents	1 (0.2%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Tumour pain	2 (0.4%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Acute coronary syndrome	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	1 (0.2%)	0 (0%)
Anaphylactic reaction	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Aphasia	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	1 (0.2%)	0 (0%)	0 (0%)
Atrial tachycardia	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	1 (0.2%)	0 (0%)	0 (0%)
Blood sodium decreased	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	1 (0.2%)	0 (0%)	0 (0%)
Bone marrow failure	1 (0.2%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Cataract	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	1 (0.2%)	0 (0%)	0 (0%)
Catheter site infection	1 (0.2%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Cerebral haemorrhage	1 (0.2%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Cerebrovascular accident	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)
Colitis	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Diverticulitis	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)
Dyskinesia	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)
Ear infection	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)
Escherichia sepsis	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Faecal volume increased	0 (0%)	2 (0.4%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Gastric haemorrhage	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	1 (0.2%)	0 (0%)	0 (0%)

	Chemo alone				Chemo + SIRT			
Event Term	1 and 2	3	4	5	1 and 2	3	4	5
Gastroenteritis radiation	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Gastrointestinal pain	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	1 (0.2%)	0 (0%)	0 (0%)
Heart rate irregular	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	1 (0.2%)	0 (0%)	0 (0%)
Hepatic encephalopathy	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (0.4%)	0 (0%)	0 (0%)
Hepatic failure	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	1 (0.2%)
Hip fracture	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	1 (0.2%)	0 (0%)	0 (0%)
Hypovolaemia	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	1 (0.2%)	0 (0%)	0 (0%)
Jaundice	0 (0%)	2 (0.4%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Jaundice cholestatic	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (0.4%)	0 (0%)	0 (0%)
Left ventricular dysfunction	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)
Lobar pneumonia	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)
Malnutrition	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	1 (0.2%)	0 (0%)
Metastatic pain	0 (0%)	2 (0.4%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Muscle strain	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	1 (0.2%)	0 (0%)	0 (0%)
Pathological fracture	0 (0%)	2 (0.4%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Performance status decreased	1 (0.2%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Peripheral artery thrombosis	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	1 (0.2%)	0 (0%)
Peritonitis	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	1 (0.2%)
Pneumonia aspiration	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)
Pneumonitis	0 (0%)	0 (0%)	2 (0.4%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Pneumothorax	1 (0.2%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Portal hypertension	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Rectal stenosis	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Respiratory failure	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)
Skin exfoliation	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)
Small intestinal obstruction	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	1 (0.2%)	0 (0%)
Spinal fracture	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Suicidal ideation	1 (0.2%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Venous thrombosis limb	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)
Abdominal sepsis	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Abdominal strangulated hernia	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Abscess limb	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Activated partial thromboplastin time	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Acute respiratory distress syndrome	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Alkalosis	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Amylase increased	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Anastomotic complication	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Anastomotic leak	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Anorectal infection	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Arterial injury	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Atrial flutter	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Atrioventricular block complete	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Bile duct stone	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Biliary tract infection	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Blood bicarbonate increased	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Blood bilirubin abnormal	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)

	Chemo alone				Chemo + SIRT			
Event Term	1 and 2	3	4	5	1 and 2	3	4	5
Blood creatine phosphokinase increased	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Breast cancer	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Bronchial obstruction	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Cardiac arrest	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Cardiotoxicity	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Cerebellar syndrome	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Cerebral infarction	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Cerebral ischaemia	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Cholecystitis acute	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Cholelithiasis	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Clostridium difficile infection	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Colon neoplasm	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Colonic abscess	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Contrast media allergy	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Contrast media reaction	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Deep vein thrombosis postoperative	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Device related sepsis	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Diabetes mellitus inadequate control	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Diabetic complication	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Diabetic ketoacidosis	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Duodenal perforation	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Duodenal ulcer haemorrhage	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Dyslipidaemia	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Enteritis infectious	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Enterococcal infection	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Enterococcal sepsis	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)
Erythema multiforme	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Escherichia bacteraemia	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Escherichia urinary tract infection	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Face injury	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Faecaloma	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Femoral artery occlusion	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Femoral neck fracture	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Gastritis atrophic	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Gastritis erosive	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Gastroduodenitis	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Gastroenteritis salmonella	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Gastrointestinal surgery	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Glaucoma surgery	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Granulocyte count decreased	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Helicobacter test positive	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Hepatic cirrhosis	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Hepatic infarction	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Hepatic vein thrombosis	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Hepatitis C	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Hernia pain	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Hydrocele	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)

	Chemo alone				Chemo + SIRT			
Event Term	1 and 2	3	4	5	1 and 2	3	4	5
Hyperparathyroidism	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Hypochloraemia	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Hypovolaemic shock	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Infusion site thrombosis	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Intestinal anastomosis complication	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Intestinal ischaemia	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Ischaemia	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Ischaemic stroke	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Klebsiella sepsis	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Large intestinal stenosis	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Lhermitte's sign	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Lipase increased	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Liver function tests abnormal	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Loss of consciousness	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Lower respiratory tract infection viral	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Lung abscess	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Malignant ascites	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Muscle haemorrhage	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Neutropenic colitis	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Neutropenic sepsis	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)
Obstruction	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)
Oedema mouth	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Oesophageal stenosis	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Oesophagitis haemorrhagic	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Orchitis	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Parainfluenzae virus infection	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Pelvic abscess	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Perihepatic abscess	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Peripheral artery stenosis	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Peripheral embolism	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Peroneal nerve palsy	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Pneumonia fungal	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Pneumonia klebsiella	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Post procedural diarrhoea	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Pseudomonal bacteraemia	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)
Pulmonary embolism	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Pulmonary infarction	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Pulmonary oedema	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Pyelonephritis	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Rectal abscess	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Renal injury	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Retinal detachment	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Salmonellosis	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Speech disorder	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Splenic infarction	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Staphylococcal bacteraemia	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Stress cardiomyopathy	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Suicide attempt	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

	Chemo alone				Chemo + SIRT			
Event Term	1 and 2	3	4	5	1 and 2	3	4	5
Supraventricular tachycardia	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Surgery	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Thyroid cancer	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Troponin increased	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Upper limb fracture	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Urinary tract obstruction	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Urine output decreased	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)
Vessel puncture site thrombosis	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Volvulus of small bowel	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Wound evisceration	0 (0%)	1 (0.2%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

[1] All grade 1-2 occurring in at least 10% of patients and all grades 3,4,5

Table S10: Grade 5 AEs in the as-treated population during the main safety window [1]

System organ class	Event Term	Chemotherapy (n=571)	Chemotherapy + SIRT (n=507)
Number of patients experiencing a grade 5 adverse event		11	10
Number of grade 5 adverse events[2]		12	12
Blood and lymphatic system disorders	Febrile neutropenia	0	1
	Neutropenia	1	0
Cardiac disorders	Acute myocardial infarction	1	0
	Cardiac arrest	1	0
Gastrointestinal disorders	Intestinal perforation	0	1
	Large intestine perforation	1	0
General disorders and administration site conditions	General physical health deterioration	0	1
Hepatobiliary disorders	Hepatic failure	0	1
	Portal vein thrombosis	0	1
Infections and infestations	Escherichia sepsis	1	0
	Lung abscess	1	0
	Neutropenic sepsis	1	0
	Peritonitis	0	1
	Pneumonia	0	1
	Respiratory tract infection	1	0
Injury, poisoning and procedural complications	Radiation hepatitis	0	2
	Toxicity to various agents	1	0
Metabolism and nutrition disorders	Diabetic complication	1	0
Nervous system disorders	Cerebral haemorrhage	1	0
Respiratory, thoracic and mediastinal disorders	Chronic obstructive pulmonary disease	0	1
	Dyspnoea	0	1
	Pneumonia aspiration	1	0
	Respiratory failure	0	1

[1]Adverse events up to 28 days after stopping protocol chemotherapy or seven months whichever was sooner
[2]Three patients had two grade 5 adverse event terms recorded in the database. One on the chemotherapy arm and two on the chemotherapy + SIRT arm.

Table S11: Summary of patients experiencing at least one SAE and its relatedness to treatment

		Combined, safety population		
		Chemotherapy (n=571)	Chemotherapy + SIRT (n=507)	Overall (n=1078)
Had at least one SAE	Yes	244 (42.7%)	274 (54.0%)	518 (48.1%)
	No	327 (57.3%)	233 (46.0%)	560 (51.9%)
Had at least one SAE related to Chemo	Yes	141 (24.7%)	165 (32.5%)	306 (28.4%)
	No	430 (75.3%)	342 (67.5%)	772 (71.6%)
Had at least one SAE related to SIRT	Yes	1 (0.2%)	83 (16.4%)	84 (7.8%)
	No	570 (99.8%)	424 (83.6%)	994 (92.2%)

Table S12. Cause of death by treatment group (n=844)

		Chemo alone (n=411)	Chemo + SIRT (n=433)	Overall (n=844)
Cause of Death	Progressive disease/CRC	290 (70.6%)	304 (70.2%)	594 (70.4%)
	Cancer (unspecified) related	7 (1.7%)	11 (2.5%)	18 (2.1%)
	Other disease related	10 (2.4%)	8 (1.8%)	18 (2.1%)
	Organ failure	12 (2.9%)	12 (2.8%)	24 (2.8%)
	Treatment related	3 (0.7%)	8 (1.8%)	11 (1.3%)
	Other	24 (5.8%)	32 (7.4%)	56 (6.6%)
	Unknown	65 (15.8%)	58 (13.4%)	123 (14.6%)

Table S13: HRQoL summaries: mean EQ-5D utility values at baseline and follow-up points, combined FOXFIRE, SIRFLOX and FOXFIRE-Global trials, using US utility tariff

	Chemo +SIRT	**Chemo alone**	**Difference (base-line adjusted)**	**Lower /Upper CI**	**p-value**	**FOXFIRE (Responses, total alive, percentage)**		**FOXFIRE Global (Responses, total alive, percentage)**		**SIRFLOX (Responses, total alive, percentage)**		**POOLED (Responses, total alive, percentage)**	
						Sirt	**No Sirt**	**Sirt**	**No Sirt**	**Sirt**	**No Sirt**	**Sirt**	**No Sirt**
Base-line	0.837	0.840				159/182 (87%)	162/182 (89%)	103/105 (98%)	102/104 (98%)	248/267 (93%)	243/263 (92%)	510/554 (92%)	507/549 (92%)
2-3 months	0.828	0.846	-0.021	-0.040/-0.001	0.038	136/176 (77%)	137/178 (77%)	80/100 (80%)	85/99 (86%)	215/260 (83%)	195/259 (75%)	431/536 (80%)	417/536 (78%)
6 months	0.823	0.836	-0.019	-0.045/0.007	0.144	13/162 (8%)	11/171 (6%)	78/97 (80%)	74/94 (79%)	169/243 (70%)	162/252 (64%)	260/502 (52%)	247/517 (48%)
12 months	0.831	0.841	-0.023	-0.050/0.004	0.096	84/132 (64%)	73/141 (52%)	57/85 (67%)	53/85 (62%)	112/213 (53%)	89/222 (40%)	253/430 (59%)	215/448 (48%)
24 months	0.810	0.814	-0.013	-0.069/0.044	0.664	41/73 (56%)	37/80 (46%)	12/62 (19%)	16/59 (27%)	32/135 (24%)	21/146 (14%)	85/270 (31%)	74/285 (26%)

* Completion rate = number of valid responses as a percentage of total known to be alive

Table S14: List of sites, principal investigators and number of patients recruited

number of PTs	Study	Principal Investigator	Hospital Name	City	Country
44	FOXFIRE	Prof Ricky Sharma/Dr Andrew Weaver	Churchill Hospital	Oxford	UK
41	FOXFIRE	Dr Harpreet Wasan	**(Imperial College Healthcare NHS Trust)**	London	UK
36	SIRFLOX	Dr. Peter Gibbs	Sunshine Hospital	St Albans	Australia
30	SIRFLOX	Dr. Chris Jackson Prof. David Perez (from 7Mar08 to 8Jan16)	Dunedin Hospital	Dunedin	New Zealand
29	FOXFIRE	Dr Jamie Mills	Nottingham City Hospital	Nottingham	UK
28	SIRFLOX	Prof. Michael Findlay	Auckland Hospital	Auckland	New Zealand
28	FOXFIRE	Dr Charles Wilson	Addenbrookes Hospital	Cambridge	UK
27	SIRFLOX	Dr. Guy Van Hazel	Mount Medical Center	Perth	Australia
26	FOXFIRE	Dr Richard Adams	Velindre Hospital	Cardiff	UK
23	FOXFIRE	Dr Amir Montazeri	Royal Liverpool University Hospital	Liverpool	UK
23	FOXFIRE	Dr Daniel Swinson	St James's University Hospital	Leeds	UK
20	SIRFLOX	Prof. Bridget Robinson	Christchurch Hospital	Christchurch	New Zealand
20	SIRFLOX	Dr. Andrew Strickland	Monash Medical Centre	Bentleigh East	Australia
20	FOXFIRE	Dr Ewan Brown	Western General Hospital	Edinburgh	UK
20	FOXFIRE	Dr Maher Hadaki: 28May2012 Dr Harpreet Wasan: 27Feb2015	Wexham Park Hospital	Slough	UK
18	SIRFLOX	Prof. Guy Van Hazel	Sir Charles Gairdner Hospital	Nedlands	Australia
18	FOXFIRE	Dr Greg Wilson	Christie Hospital	Manchester	UK
15	SIRFLOX	Prof. Jens Ricke	Universitaetsklinikum Magdeburg, Klinik für Radiologie und Nuklearmedizin	Magdeburg	Germany
14	SIRFLOX	Dr. Thomas Ferguson Dr. David Ransom (from 12Dec07 to 21Dec11)	Fiona Stanley Hospital	Murdoch	Australia
13	SIRFLOX	Dr. Hendrik Kröning	Schwerpunktpraxis für Hämatologie und Onkologie	Magdeburg	Germany
13	SIRFLOX	Dr. Javier Rodriguez	Clinica Universitaria de Navarra	Pamplona	Spain
13	FOXFIRE	Dr Rebecca Muirhead: 14Dec2012 Dr Sarah Lowndes: 31Jul2015	Great Western Hospital	Swindon	UK
12	FOXFIRE Global	Dr. Marc Pracht Dr. Eveline Boucher (from 3Dec13 to 24Feb15)	Centre Eugéne Marquis	Rennes cedex	France
11	SIRFLOX	Prof. Adi Shani Dr. Ido Wolf (until 17Apr12)	Sheba Medical Center	Tel-Hashomer	Israel
11	FOXFIRE	Dr Paul Ross	Kings Health Partnership (Guys)	London	UK

number of PTs	Study	Principal Investigator	Hospital Name	City	Country
11	FOXFIRE	Dr Joanne Hornbuckle	Weston Park Hospital	Sheffield	UK
10	SIRFLOX	Dr. Vinod Ganju	Peninsula and South Eastern Haematology and Oncology Group	Frankston	Australia
10	SIRFLOX	Dr. Euan Walpole	Princess Alexandra Hospital	Woolloongabba	Australia
10	SIRFLOX	Dr. Marc Pracht Dr. Evelyn Boucher (until 27Feb2015)	Comprehensive Cancer Centre Eugéne Marquis	Rennes	France
10	FOXFIRE Global	Prof. Guy Van Hazel	Sir Charles Gairdner Hospital	Nedlands	Australia
9	SIRFLOX	Dr. Adeel Kaiser Dr. Michael Chuong (from 6May15 to 28Jun15) Dr. Pradip Amin (from 24Jul09 to 22Nov11) Dr. Micheal Garofalo (from 20Mar08 to 24Sep09) Dr. Navesh Sharma (from 22Nov11 to 06May15)	University of Maryland Medical Center	Baltimore	USA
9	SIRFLOX	Dr. Ravit Geva Dr. Einat Shacham-Shmueli (until 01Aug12)	TA Sourasky Medical Center	Tel Aviv	Israel
9	SIRFLOX	Dr. Norman Isaac Heching Dr. Thomas Tichler (until 28Feb14)	Shaare-Zedek Medical Center	Jerusalem	Israel
8	SIRFLOX	Dr. Richard Isaacs	Palmerston North Hospital	Palmerston North	New Zealand
8	SIRFLOX	Dr. Alex Powell/Dr. Joe Cardaci	Hollywood Private Hospital	Nedlands	Australia
8	FOXFIRE Global	Dr. Madhu Singh	Barwon Health	Geelong	Australia
8	FOXFIRE Global	Dr. Ana Ruiz Casado	Hospital Universitario Puerta de Hierro Majadahonda	Madrid	Spain
8	FOXFIRE	Dr Andrew Bateman	Southampton General Hospital	Southampton	UK
7	SIRFLOX	Dr. Paul Eliadis	Wesley Medical Centre	Milton	Australia
7	SIRFLOX	Dr. Eric Wang/Dr. Seungjean Chai Dr. Frenette (until 30Jun16) Dr. Steven Limentani (from 08Apr11 to 17Jul15)	Carolinas Health System	Charlotte	USA
7	SIRFLOX	Dr. Yi Jen Chen Dr. Stephen Shibata (until 22Apr12)	City of Hope	Duarte	USA
7	SIRFLOX	Dr. Els Monsaert	AZ Maria Middelares	Gent	Belgium
7	FOXFIRE Global	Dr. Peter Gibbs	Sunshine Hospital	St Albans	Australia
7	FOXFIRE	Dr Andrew Weaver	**Buckinghamshire Healthcare NHS Trust**	Buckinghamshire	UK
6	SIRFLOX	Prof. Yon-Dschun Ko	Johanniterkrankenhaus Bonn	Bonn	Germany
6	SIRFLOX	Dr. Stefan Pluntke	Kliniken Essen Mitte, Evang. Huyssens-Stiftung/Knappschaft GmbH	Essen	Germany
6	SIRFLOX	Dr. Marc Polus	C.H.U. Sart-Tilman	Liège	Belgium
6	SIRFLOX	Prof. Julien Taieb	Hôpital Européen Georges Pompidou (HEGP)	Paris	France
6	FOXFIRE Global	Dr. Anne O'Donnell	Wellington Hospital	Wellington	New Zealand
6	FOXFIRE Global	Dr. Morteza Aghmesheh	Southern Medical Day Care Centre	Wollongong	Australia
6	FOXFIRE Global	Dr. Kynan Feeney	St John of God Murdoch Hospital	Murdoch	Australia
6	FOXFIRE Global	Dr. Jin Tung Liang	National Taiwan University Hospital	Taipei	Taiwan

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6	FOXFIRE	Dr Rubin Soomal: 29-Aug2011 Dr Liz Sherwin: 23Sep2015	Ipswich Hospital	Ipswich	UK
5	SIRFLOX	Dr. Nick Pavlakis	Royal North Shore Hospital	St Leonards	Australia
5	SIRFLOX	Dr. Nimit Singhal Dr. Michael Brown (from 21Jan08 to 15Aug10)	Royal Adelaide Hospital	Adelaide	Australia
5	SIRFLOX	Dr. Robert Martin	University of Louisville Hospital	Louisville	USA
5	SIRFLOX	Dr. Andreas Kaubisch	Montefiore Medical Center	Bronx, NY	USA
5	SIRFLOX	Dr. Matthew Holtzman	University of Pittsburgh Medical Center	Pittsburgh	USA
5	SIRFLOX	Prof. Dr. med. Hanno Riess	CharitéCentrum 14 für Tumormedizin - Med. Klinik mit Schwerpunkt	Berlin	Germany
5	SIRFLOX	Dr. Denis Smith/Dr. Eric Terrebonne	CHU de Bordeaux	Bordeaux/Pessac	France
5	FOXFIRE Global	Dr. Vinod Ganju	Peninsula and South Eastern Haematology and Oncology Group	Frankston	Australia
5	FOXFIRE Global	Dr. Lionel Lim	Maroondah Hospital	Ringwood East	Australia
5	FOXFIRE Global	Dr. Prasad Cooray	Box Hill Hospital	Box Hill	Australia
5	FOXFIRE Global	Dr. Marco Matos	Gold Coast University Hospital	Southport	Australia
5	FOXFIRE Global	Dr. Aurélie Ferru	CHU de Poitiers, Pôle régional de cancérologie	Poitiers	France
5	FOXFIRE Global	Dr. Ravit Geva	TA Sourasky Medical Center	Tel Aviv	Israel
5	FOXFIRE Global	Dr. Hubert Ayala	Hadassah Medical Center	Jerusalem	Israel
5	FOXFIRE	Dr Colin Purcell	Belfast City Hospital	Belfast	UK
5	FOXFIRE	Dr Axel Walther	Bristol Haematology & Oncology Centre	Bristol	UK
5	FOXFIRE	Mr Matthew Metcalfe	Leicester Royal Infirmary	Leicester	UK
5	FOXFIRE	Dr Andreas Polychronis	Lister Hospital	Stevenage	UK
5	FOXFIRE	Dr Fiona Lofts	St Georges Hospital	London	UK
4	SIRFLOX	Dr. Jenny Shannon	Nepean Hospital Nepean Cancer Care Centre	Kingswood	Australia
4	SIRFLOX	Prof. Eva Segelov	St Vincent's Hospital	Darlinghurst	Australia
4	SIRFLOX	Dr. Philip James	Maroondah Hospital	Ringwood East	Australia
4	SIRFLOX	Dr. Marco Matos	Gold Coast University Hospital	Southport	Australia
4	SIRFLOX	Dr. Seza Gulec	Florida International University	North Miami Beach	USA
4	SIRFLOX	Dr. Ursula Vehling-Kaiser	Internistische Gemeinschaftspraxis	Landshut Altstadt	Germany
4	SIRFLOX	Prof. Dr. Volker Heinemann	Klinikum der Universitaet Muenchen, Klinikum Großhadern	Muenchen	Germany
4	SIRFLOX	Prof. Klaus Tatsch	Klinikum Karlsruhe, Städtisches Klinikum Karlsruhe gGmbH	Karlsruhe	Germany
4	SIRFLOX	Prof. Karen Geboes	Universiteit Ziekenhuis Gent	Gent	Belgium
4	SIRFLOX	Dr. Ruth Vera Garcia	Hospital de Navarra	Pamplona	Spain
4	SIRFLOX	Dr. Alex Beny	Rambam Health Care Campus	Haifa	Israel
4	FOXFIRE Global	Prof. Michael Findlay	Auckland University	Auckland	New Zealand
4	FOXFIRE Global	Dr. Mathew Burge	Royal Brisbane and Women's Hospital	Herston	Australia

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4	FOXFIRE Global	Dr. Tom Ferguson	Royal Perth Hospital	Murdoch	Australia
4	FOXFIRE Global	Dr. Norman Isaac Heching Dr. Thomas Tichler (until 28Feb14)	Shaare-Zedek Medical Center	Jerusalem	Israel
4	FOXFIRE Global	Kyran Dowling, MD Charles Bowers, MD (until 26Oct15)	Spartanburg Regional Healthcare	Spartanburg	USA
4	FOXFIRE	Dr Ian Chau	**Royal Marsden NHS foundation trust**	London	UK
3	SIRFLOX	Dr. Peter Gibbs	Royal Melbourne Hospital	Melbourne	Australia
3	SIRFLOX	Prof. Timothy Price	Queen Elizabeth Hospital	Woodville South	Australia
3	SIRFLOX	Dr. Federico Sanchez Dr. Jacob Frick (from 11Jul11 to 12Jan15) Dr. Daniel Bloomgarden (from 11Jul11 to 1Jul14)	Aurora Advanced Healthcare	Wauwatosa	USA
3	SIRFLOX	Dr. James Carlisle	St. Marks Hospital	Salt Lake City	USA
3	SIRFLOX	Dr. med. Jorge Ramon Urrico Riera Knorrenschild	Universitätsklinikum Gießen und Marburg GmbH	Marburg	Germany
3	SIRFLOX	Prof. Frank Lammert	Universitätsklinikum des Saarlandes	Homburg/Saar	Germany
3	SIRFLOX	Dr. Karsten Ridwelski	Klinikum Magdeburg gGmbH	Magdeburg	Germany
3	SIRFLOX	Prof. Tilmann Sauerbruch	Universitätsklinik Bonn, Medizinische Klinik und Poliklinik I	Bonn	Germany
3	SIRFLOX	Prof. Thomas Vogl	Klinikum der Johann Wolfgang Goethe-Universität Frankfurt am Main	Frankfurt am Main	Germany
3	SIRFLOX	Dr. Amélie Deleporte Prof. Alain Hendlisz (from 1Feb12 to 2May12	Institut Jules Bordet	Brussels	Belgium
3	SIRFLOX	Prof. Mark Peeters	UZ Antwerpen	Edegem	Belgium
3	SIRFLOX	Prof. Jacques Balosso Dr. Christine Rebischung (until 16Aug 14)	Centre Hospitalier Universitaire de Grenoble C.H.U	La Tronche	France
3	SIRFLOX	Dr. Samy Louafi	Centre Hospitalier General de Longjumeau	Longjumeau	France
3	SIRFLOX	Dr. Salomon Stemmer	Beilinson Hospital	Petak Tikva	Israel
3	FOXFIRE Global	Dr. Chris Jackson	Dunedin Hospital	Dunedin	New Zealand
3	FOXFIRE Global	Dr. Louise Nott	Royal Hobart Hospital	Hobart	Australia
3	FOXFIRE Global	Dr. Andrew Strickland	Monash Medical Centre	Bentleigh East	Australia
3	FOXFIRE Global	Dr. Craig Underhill	Border Medical Oncology Research Unit	Albury	Australia
3	FOXFIRE Global	Dr. Hendrik Kröning	Schwerpunktpraxis für Hämatologie und Onkologie	Magdeburg	Germany
3	FOXFIRE Global	Dr. Els Monsaert	AZ Maria Middelaress	Gent	Belgium
3	FOXFIRE Global	Prof Julien Taieb	Hôpital Européen Georges Pompidou (HEGP)	Paris	France
3	FOXFIRE Global	Dr. Samy Louafi	Centre Hospitalier General de Longjumeau	Longjumeau	France
3	FOXFIRE Global	Dr. Gianluca Masi	Ospedale Santa Chiara	Pisa	Italy
3	FOXFIRE Global	James Bui, MD	University of Illinois at Chicago	Chicago	USA
3	FOXFIRE Global	Francis Facchini, MD	Adventist Hinsdale Hospital	Hinsdale	USA

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3	FOXFIRE Global	Prof. HAN Sae Won	Seoul National University Hospital	Seoul	Korea
3	FOXFIRE	Dr Astrid Mayer	Royal Free Hospital London	London	UK
2	SIRFLOX	Dr. Anne O'Donnell	Wellington Hospital	Wellington	New Zealand
2	SIRFLOX	Dr. Winston Liauw	St George Hospital	Kogarah	Australia
2	SIRFLOX	Dr. Gavin Marx	Sydney Adventist Hospital	Wahroonga	Australia
2	SIRFLOX	Dr. Louise Nott	Royal Hobart Hospital	Hobart	Australia
2	SIRFLOX	Dr. Randall Smith/Dr. Grant Seeger	Altru Health Systems	Grand Forks	USA
2	SIRFLOX	Dr. Francis Facchini/Dr. James Hannigan/Dr. Elyse Schneiderman	Adventist Midwest Health/Hinsdale Hospital	Hinsdale	USA
2	SIRFLOX	Dr. Michael Gordon	Pinnacle Hematology Oncology	Scottsdale	USA
2	SIRFLOX	Dr. James Bui/Dr. Howard Ozer	University of Illinois at Chicago	Chicago	USA
2	SIRFLOX	Dr. Bruna Angelelli Dr. Andrea Martoni (until 01 Sept 2012)	Ospedale Sant'Orsola-Malpighi	Bologna	Italy
2	SIRFLOX	Dr. Oliver J. Stötzer	Hämato-onkologische Gemeinschaftspraxis und Tagesklinik	München	Germany
2	SIRFLOX	Dr. Klemens Scheidhauer	Klinikum rechts der Isar der TU München, Nuklearmedizinische Klinik u. Poliklinik,	München	Germany
2	SIRFLOX	Prof. Thomas Helmberger	Klinikum Bogenhausen, Städtisches Klinikum München GmbH	Muenchen	Germany
2	FOXFIRE Global	Dr. Nimit Singhal	Royal Adelaide Hospital	Adelaide	Australia
2	FOXFIRE Global	Prof. Maike De Wit	Vivantes Klinikum Neukölln Klinik für Innere Medizin-Hämatologie und Onkologie	Berlin	Germany
2	FOXFIRE Global	Dr. Koenraad Hendrickx Dr. Marc De Man (from 25Jul13 to 31 Dec13)	OL Vrouw Ziekenhuis	Aalst	Belgium
2	FOXFIRE Global	Prof. Alain Hendlisz Dr. Amelie Deleporte (from 10Sep13 to 31Jan15)	Institut Jules Bordet	Brussels	Belgium
2	FOXFIRE Global	Dr.Denis Smith and Dr.Eric Terrebonne	CHU de Bordeaux (Hôpital Saint Andre & Hôpital du Haut-Levêque)	Bordeaux/Pessac	France
2	FOXFIRE Global	Prof. Adi Shani	Sheba Medical Center - Governmental Hospital	Tel Hashomer	Israel
2	FOXFIRE Global	Dr. Cristina Granetto	Ospedale Santa Croce e Carle di Cuneo	Confreria (CN)	Italy
2	FOXFIRE Global	Dr. Bruna Angelelli	Policlinico Sant'Orsola Malpighi	Bologna	Italy
2	FOXFIRE Global	Dr. Antonio Trogu Dr. Gianmauro Numico (08Oct13 to 11Aug15)	Azienda USL della Valle d'Aosta	Aosta	Italy
2	FOXFIRE Global	Dr. Ruth Vera Garcia	Complejo Hospitalario de Navarra	Pamplona	Spain
2	FOXFIRE Global	Dr. Rosa Maria Fragoso	Instituto Português de Oncologia do Porto Francisco Gentil, E.P.E. (IPO Porto)	Porto	Portugal
2	FOXFIRE Global	James Carlisle, MD	St. Mark's Hospital	Salt Lake City	USA
2	FOXFIRE Global	Andreas Kaubisch, MD	Montefiore Medical Center	Bronx	USA

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2	FOXFIRE Global	Matthew Holtzman, MD	University of Pittsburgh Medical Center	Pittsburgh	USA
2	FOXFIRE Global	Prof. KIM Yeul Hong	Korea University Anam Hospital	Seoul	Korea
2	FOXFIRE	Dr Tamas Hickish	Royal Bournemouth	Bournemouth	UK
2	FOXFIRE	Dr Sebastian Cummins	Royal Surrey County Hospital	Guildford	UK
1	SIRFLOX	Dr. Matthew Burge	Royal Brisbane & Women's Hospital	Herston	Australia
1	SIRFLOX	Dr. Chris Karapetis	Flinders Medical Center	Bedford Park	Australia
1	SIRFLOX	Prof. Timothy Price	Lyell McEwin Hospital	Elizabeth Vale	Australia
1	SIRFLOX	Dr. William Rilling/Dr. Benjamin George	Medical College of Wisconsin - Froedtert Hospital	Milwaukee	USA
1	SIRFLOX	Dr. Andrew Coveler Dr. Siddarth Padia (until 08Aug14) Dr. Samuel Whiting (from 10Nov11 to 03May12)	University of Washington	Seattle	USA
1	SIRFLOX	Dr. Michael Savin/Dr. Jeffrey Margolis	William Beaumont Hospital	Royal oak	USA
1	SIRFLOX	Dr. med. Arnd Nusch	Praxis für Hämatologie und Internistische Onkologie	Velbert	Germany
1	SIRFLOX	Prof. Dr. med. Harald-Robert Bruch	Praxiskooperation Bonn, Fachärzte für Innere Medizin	Bonn	Germany
1	SIRFLOX	Dr. Gerald Gehbauer	Onkologische Praxis Dr. Gerald Gehbauer	Ingolstadt	Germany
1	SIRFLOX	Dr. Koen Hendrickx Dr. Marc De Man (from 23Jun11 to 31Dec13)	Onze Lieve Vrouw Kiekenhuis	Aalst	Belgium
1	SIRFLOX	Dr. Thierry Delaunoit	Hopital de Jolimont	Haine-Saint-Paul	Belgium
1	SIRFLOX	Dr. Veerle Moons	Imelda Ziekenhuis	Bonheiden	Belgium
1	SIRFLOX	Dr. Michael Craninx	AZ Heilige Familie	Reet	Belgium
1	SIRFLOX	Dr. Michael Ferrante	AZ Sint-Maarten, Gastro-enterologie	Mechelen	Belgium
1	SIRFLOX	Prof. Patrick Chevallier	HÔPITAL de l'Archet II	Nice	France
1	FOXFIRE Global	Dr. Richard Issacs	Palmerston North Hospital	Palmerston North	New Zealand
1	FOXFIRE Global	Dr. Andrew Strickland	South Eastern Hospital	Noble Park	Australia
1	FOXFIRE Global	Dr. Euan Walpole	Princess Alexandra Hospital	Woolloongabba	Australia
1	FOXFIRE Global	Prof. Christoph Bremer	St. Franziskus Hospital Muenster	Muenster	Germany
1	FOXFIRE Global	Prof. Marc Peeters	Antwerp University Hospital	Antwerp, Edegem	Belgium
1	FOXFIRE Global	Dr. Marc Polus	CHU Sart Tilman	Liege	Belgium
1	FOXFIRE Global	Dr. Pascal Hammel Prof. Sandrine Faivre (from 31Oct13 to 19Jun14)	Hôpital Beaujon	Clichy	France
1	FOXFIRE Global	Dr. Aurelie Durand Dr. Christine Rebischung (from 04Oct13 to 16Aug 14)	Hôpital Albert Michallon	CHU Grenoble	France
1	FOXFIRE Global	Dr. Alex Beny	Rambam Health Care Campus	Haifa	Israel
1	FOXFIRE Global	Dr. Stefania Mosconi	Ospedali Riuniti di Bergamo	Bergamo	Italy

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1	FOXFIRE Global	Dr. Federico Sanchez Dr. Martin Crain Dr. Jacob Frick (until 12Jan15) Dr. Daniel Bloomgarden (until 1Jul14)	Aurora St. Luke's Medical Center	Milwaukee	USA
1	FOXFIRE Global	Dr. Adeel Kaiser Dr. Michael Chuong (from 6May15 to 28Jun15) Dr. Navesh Sharma (until 06May15)	University of Maryland	Baltimore	USA
1	FOXFIRE Global	Dr. Eric Wang/Dr. Seungjean Chai Dr. Frenette (until 30Jun16) Dr. Steven Limentani (from 08Apr11 to 17Jul15)	Carolinas Medical Center	Charlotte	USA
1	FOXFIRE Global	Dr. Mark Westcott/Lynn Ratner, MD	Lenox Hill Hospital	New York	USA
1	FOXFIRE Global	Patrick Boland Renuka Iyer, MD (until 3Mar14)	Roswell Park Cancer Institute	Buffalo	USA
1	FOXFIRE Global	Dr. Miklos Auber Patricia Stoltzfus, MD (until 30Apr15)	West Virginia University Healthcare	Morgantown	USA
1	FOXFIRE Global	Steven Ades, MD	University of Vermont Medical Center (formerly Fletcher Allen Healthcare)	Burlington	USA
1	FOXFIRE Global	Dr. Iain Tan	National Cancer Centre	Singapore	Singapore
1	FOXFIRE Global	Dr. Jin Hwang Liu	Taipei Veterans General Hospital	Taipei	Taiwan

Investigators/Trial Committees

DSMC: Stephen Ackland, Richard Wilson, Matthew Law, John Wagstaff, Desmond Yip and Gareth Griffiths

TSC: Mike Bradburn, William Allum and Leslie Samuel.

The FOXFIRE Trial Management and Quality Assurance Group: Adil Al-Nahhas, Dave Berry, Ian Chau, Luise Dunham, David Kerr, Nas Khan, Val Lewington, Rachel Midgley, Bruno Morgan, Sarah Pearson, Anne Roberts, Will Steward, Paul Tait, Greg Wilson, Andy Wotherspoon.

FOXFIRE Health Economists: Alastair Gray, Jane Wolstenholme.

The FOXFIRE Study Group: Richard Adams, Andrew Bateman, Claire Blesing, Ewan Brown, Ian Chau, Sebastian Cummins, David Cunningham, Stephen Falk, Maher Hadaki, Marcia Hall, Tamas Hickish, Joanne Hornbuckle, Fiona Lofts, Sarah Lowndes, Astrid Mayer, Matthew Metcalfe, Gary Middleton, Jamie Mills, Amir Montazeri, Rebecca Muirhead, Andreas Polychronis, Colin Purcell, Paul Ross, Liz Sherwin, David Smith, Rubin Soomal, Daniel Swinson, Axel Walther, Andrew Weaver, Charles Wilson, Greg Wilson. We would also like to thank the University of Oxford statistician Susan Dutton for her contribution to the FOXFIRE study.

The SIRFLOX and FOXFIRE-Global Study Group: Steven Ades, Morteza Aghmesheh, Pradip Amin, Bruna Angelelli, Miklos Auber, Jacques Balosso, Alex Beny, Daniel Bloomgarden, Patrick Boland, Eveline Boucher, Christoph Bremer, Michael Brown, Harald-Robert Bruch, James Bui, Matthew Burge, Giuseppe Cardaci, James

Carlisle, Ruiz Casado, Yi-Jen Chen, Patrick Chevallier, Michael Chuong, Stephen Clarke, Prasad Cooray, Andrew Coveler, Michel Craninx, Thierry Delanoit, Amélie Deleporte, Kyran Dowling, Aurelie Durand, Paul Eliadis, Francis Facchini, Kynan Feeney, Thomas Ferguson, Michel Ferrante, Aurelie Ferru, Michael Findlay, Maria Fragoso, Gary Frenette, Jacob Frick, Vinod Ganju, Michael Garofalo, Karen Geboes, Gerald Gehbauer, Benjamin George, Ravit Geva, Michael Gordon, Cristina Granetto, Kate Gregory, Seza Gulec, Pascal Hammel, James Hannigan, Norman Heching, Volker Heinemann, Thomas Helmberger, Alain Hendlisz, Koen Hendrickx, Matthew Holtzman, Ayala Hubert, Richard Isaacs, Christopher Jackson, Philip James, Adeel Kaiser, Chris Karapetis, Andreas Kaubisch, Yeul Hong Kim, Yon-Dschun Ko, Todd Kooy, Hendrik Kröning, Frank Lammert, Jin Tung Liang, Winston Liauw, Lionel Lim, Yoo Joo Lim, Jin Hwang Liu, Samy Louafi, Marc de Man, Jeffrey Margolis, Robert Martin, Andrea Martoni, Gavin Marx, Marco Matos, Els Monsaert, Veerle Moons, Stefania Mosconi, Louise Nott, Arnd Nusch, Anne O'Donnell, Howard Ozer, Siddarth Padia, Nick Pavlakis, Marc Peeters, David Perez, Stefan Pluntke, Marc Polus, Alex Powell, Marc Pracht, Timothy Price, Jorge Ramon, David Ransom, Christine Rebischung, Jens Ricke, Karsten Ridwelski, Hanno Riess, Jorge Ramon Riera, William Rilling, Bridget Robinson, Javier Rodríguez, Federico Sanchez, Tilmann Sauerbruch, Michael Savin, Klemens Scheidhauer, Elyse Schneiderman, Grant Seeger, Eva Segelov, Einat Shaham Schmueli, Adi Shani, Jenny Shannon, Navesh Sharma, Stephen Shibata, Nimit Singhal, Denis Smith, Randall Smith, Salomon Stemmer, Oliver Stötzer, Andrew Strickland, Julien Taieb, Iain Tan, Klaus Tatsch, Eric Terrebonne, Thomas Tichler, Antonio Trogu, Craig Underhill, Daniel Van Daele, Ursula Vehling-Kaiser, Ruth Vera-Garcia, Caterina Vivaldi, Thomas Vogl, Euan Walpole, Eric Wang, Mark Westcott, Samuel Whiting, Ido Wolf.