

Supplemental online content for:

Health-Related Quality of Life in Patients With Metastatic Colorectal Cancer Undergoing Systemic Therapy With or Without Maximal Tumor Debulking

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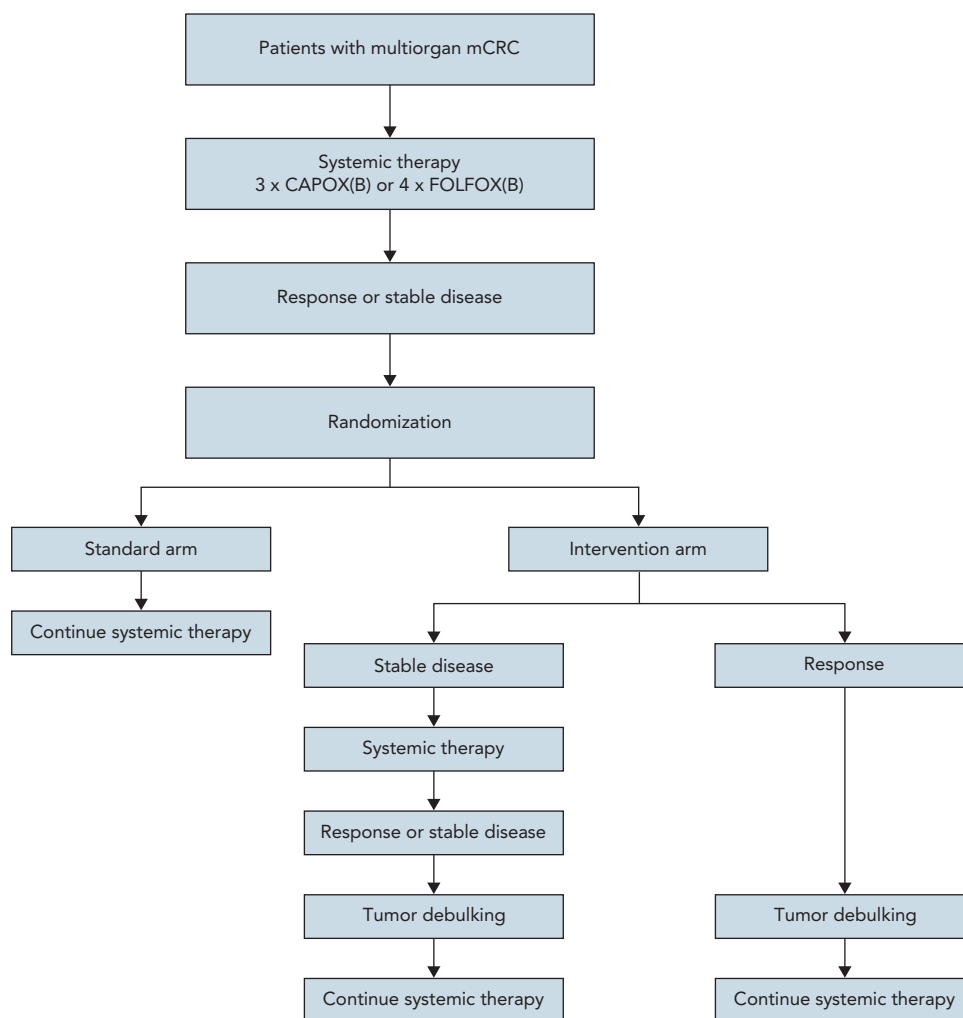
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eFigure 1. Study design for ORCHESTRA trial.

Abbreviations: CAPOX(B), capecitabine/oxaliplatin ± bevacizumab; FOLFOX(B), 5-FU/leucovorin/oxaliplatin ± bevacizumab.

eTable 1. Patient Demographics and Clinical Characteristics			
Characteristic	Total n (%)	Standard Arm n (%)	Intervention Arm n (%)
Total, N	300	152	148
Gender			
Male	203 (68)	105 (69)	98 (66)
Female	97 (32)	47 (31)	50 (34)
Age			
<65 y	158 (53)	79 (52)	79 (53)
≥65 y	137 (46)	70 (46)	67 (45)
Chronicity			
Synchronous	163 (54)	89 (59)	74 (50)
Metachronous	135 (45)	62 (41)	73 (49)
Sidedness primary tumor			
Left total	217 (72)	106 (70)	111 (75)
Rectum	123 (41)	63 (41)	60 (41)
Right	81 (27)	45 (30)	36 (24)
Primary in situ			
Yes	97 (32)	51 (34)	46 (31)
No	203 (68)	101 (66)	102 (69)
Number of metastases			
≤5	131 (44)	65 (43)	66 (45)
6–10	104 (35)	53 (35)	51 (35)
>10 or diffuse	65 (22)	34 (22)	31 (21)
Number of organs involved			
2	164 (55)	83 (55)	81 (55)
>2	133 (44)	68 (45)	65 (44)
Liver and lung metastases only			
Yes	73 (24)	36 (24)	37 (25)
No	227 (76)	116 (76)	111 (75)
CEA			
≤5 μg/L	95 (32)	52 (34)	43 (29)
>5 μg/L	205 (68)	100 (66)	105 (71)
LDH			
Normal	236 (79)	118 (78)	118 (80)
Abnormal	54 (18)	28 (18)	26 (18)
BRAF			
Mutated	20 (7)	10 (7)	10 (7)
Wild-type	201 (67)	110 (72)	91 (62)
Missing	79 (26)	32 (21)	47 (32)
KRAS			
Mutated	130 (43)	72 (47)	58 (39)
Wild-type	104 (35)	55 (36)	49 (33)
Missing	66 (22)	25 (16)	41 (28)

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eTable 1. Patient Demographics and Clinical Characteristics (cont.)

Characteristic	Total n (%)	Standard Arm n (%)	Intervention Arm n (%)
NRAS			
Mutated	14 (5)	8 (5)	6 (4)
Wild-type	191 (64)	106 (70)	85 (57)
Missing	95 (32)	38 (25)	57 (39)
MMR status			
MSI	2 (1)	1 (1)	1 (1)
MSS	166 (55)	80 (53)	86 (58)
Missing	132 (44)	71 (47)	61 (41)
Response at first evaluation			
CR	2 (1)	1 (1)	1 (1)
PR	143 (48)	73 (48)	70 (47)
SD	155 (52)	78 (51)	77 (52)
Prior treatment primary^a			
Yes	139 (46)	66 (43)	73 (49)
No	161 (54)	86 (57)	75 (51)
Previous local treatment metastases			
Yes	116 (39)	62 (41)	54 (37)
No	184 (61)	90 (59)	94 (64)

Percentages may not equal 100 due to rounding.

Abbreviations: CEA, carcinoembryonic antigen; CR, complete response; LDH, lactate dehydrogenase; MMR, mismatch repair; MSI, microsatellite instability; MSS, microsatellite stable; PR, partial response; SD, stable disease.

^aTreatment consisted of (neo)adjuvant chemotherapy and/or chemoradiation and/or radiotherapy.

eTable 2. Local Treatment Characteristics of Patients in Intervention Arm B		n (%)
Intervention arm		148 (49%)
Debulking performed		129 (87%)
Number of modalities		Median, 2 (range, 1–3)
1	Surgery only	39 (30%)
	RT only	18 (14%)
	RFA only	7 (5%)
2	Surgery and RFA	21 (16%)
	Surgery and RT	27 (21%)
	RFA and RT	6 (5%)
3	Surgery and RFA and RT	11 (9%)
Total hospital local treatment days (surgical admission, [unplanned] readmissions, RT sessions and/or percutaneous RFA treatment)		Median, 12 (IQR, 11.5)
Total unplanned readmissions		21 (16%)

Abbreviations: RFA, radiofrequency ablation; RT, radiotherapy.

eTable 3. Estimated Marginal Means EORTC QLQ-C30 and MFI per Time Point						
	Randomization	Follow-Up 1	Follow-Up 2	Follow-Up 3	Follow-Up 4	Between Group Differences Over Time β (95% CI)
EORTC QLQ-C30 summary score, mean score [SE]						
Standard arm	83.94 [1.14]	84.62 [1.22]	85.83 [1.34]	86.72 [1.47]	85.76 [1.80]	3.08 (–6.21 to 0.04); $P = .06$
Intervention arm	80.86 [1.16]	81.19 [1.27]	82.99 [1.31]	88.04 [1.53]	84.75 [1.79]	
EORTC QLQ-C30 global QoL, mean score [SE]						
Standard arm	71.07 [2.09]	67.18 [2.74]	73.62 [2.12]	75.00 [2.36]	74.66 [2.91]	2.92 (–7.81 to 1.97); $P = .24$
Intervention arm	68.15 [2.12]	64.75 [2.75]	71.88 [2.10]	77.73 [2.46]	74.76 [2.89]	
EORTC QLQ-C30 physical functioning, mean score [SE]						
Standard arm	84.85 [1.39]	84.21 [1.52]	83.19 [1.67]	84.51 [1.85]	83.11 [2.27]	3.52 (–7.45 to 0.40); $P = .08$
Intervention arm	81.32 [1.45]	80.31 [1.58]	80.97 [1.66]	85.45 [1.93]	85.07 [2.26]	
EORTC QLQ-C30 emotional functioning, mean score [SE]						
Standard arm	79.84 [1.66]	82.00 [1.75]	80.40 [1.87]	80.23 [2.04]	85.94 [2.65]	–1.01 (–3.50 to 5.52); $P = .66$
Intervention arm	80.86 [1.67]	81.80 [1.78]	80.84 [1.86]	80.54 [2.17]	85.81 [2.57]	
MFI general fatigue, mean score [SE]						
Standard arm	10.86 [0.39]	11.45 [0.42]	10.26 [0.46]	10.27 [0.50]	10.54 [0.61]	–0.87 (–0.21 to 1.96); $P = .11$
Intervention arm	11.74 [0.40]	11.56 [0.43]	11.49 [0.45]	10.10 [0.52]	10.77 [0.62]	
MFI physical fatigue, mean score [SE]						
Standard arm	11.09 [0.49]	12.11 [0.62]	10.05 [0.48]	10.49 [0.53]	9.74 [0.64]	–0.76 (–0.37 to 1.89); $P = .19$
Intervention arm	11.85 [0.50]	12.37 [0.62]	11.15 [0.48]	9.89 [0.55]	10.25 [0.64]	

Abbreviations: EORTC QLQ-C30, EORTC Quality of Life Questionnaire-Core 30; MFI, Multidimensional Fatigue Inventory; QoL, quality of life.

eTable 4. Median HRQoL and Fatigue Scores of the Intervention Group Before and After Debulking

Scale	Before Debulking (N=146)	After Debulking (N=134)	P Value ^a
EORTC QLQ-C30			
n ^b	72	72	.82
Summary score, median (IQR)	85 (20.73)	86.32 (22.95)	
n ^b	74	74	.42
Global QoL, median (IQR)	75 (25)	75 (25)	
n ^b	74	74	.14
Physical functioning, median (IQR)	86.67 (26.67)	86.67 (26.67)	
n ^b	74	74	.68
Emotional functioning, median (IQR)	83.33 (25)	83.33 (33.33)	
MFI			
n ^b	74	7	.32
General fatigue, median (IQR)	12 (7)	11 (7)	
n ^b	74	74	.61
Physical fatigue, median (IQR)	12 (7)	11 (8)	

Abbreviations: EORTC QLQ-C30, EORTC Quality of Life Questionnaire-Core 30; HRQoL, health-related quality of life; MFI, Multidimensional fatigue inventory.

^aWilcoxon signed-rank test.

^bNumber of patients based on complete cases who completed EORTC QLQ-C30/MFI questionnaire before and after intervention.