Supplementary Online Content

Cremolini C, Antoniotti C, Lonardi S, et al. Activity and safety of cetuximab plus modified FOLFOXIRI followed by maintenance with cetuximab or bevacizumab for *RAS* and *BRAF* wild-type metastatic colorectal cancer: a randomized phase 2 clinical trial. *JAMA Oncol.* Published online February 15, 2018. 10.1001/jamaoncol.2017.5314

This supplementary material has been provided by the authors to give readers additional information about their work.

eAppendix. Participating Centers and Principal Investigators

Principal Investigator	Site Name	City
Alfredo Falcone	Polo Oncologico – Ospedale Santa Chiara	Pisa
Manuela Rossi	A.O.SS. Antonio e Biagio e Cesare Arrigo	Alessandria
Sergio Frustaci	Centro di Riferimento Oncologico IRCCS	Aviano
Carmine Pinto	Ospedale Sant'Orsola	Bologna
Alberto Zaniboni	Fondazione Poliambulanza	Brescia
Francesca Valcamonico	ASST degli Spedali Civili	Brescia
Cristina Granetto	Ospedale Santa Croce e Carle	Cuneo
Teresa Gamucci	Ospedale F. Spaziani	Frosinone
Silvana Chiara	Ospedale San Martino IRCCS	Genova
Luca Gianni	Ospedale San Raffaele IRCCS	Milano
Sara Lonardi	Istituto Oncologico Veneto IRCCS	Padova
Giacomo Allegrini	Ospedale "Felice Lotti"	Pontedera
Corrado Boni	Arcispedale Santa Maria Nuova IRCSS	Reggio Emilia
Ida Pavese	Ospedale San Pietro Fatebenefratelli	Roma
Domenico Corsi	Ospedale San Giovanni Calibita Fatebenefratelli	Roma
Enrico Cortesi	Policlinico Umberto I	Roma
Giuseppe Tonini	Università Campus Biomedico	Roma
Alessandro Bertolini	Ospedale di Sondrio	Sondrio
Libero Ciuffreda	Azienda Ospedaliero–Universitaria Città della Salute e della Scienza	Torino
Giuseppe Aprile	Ospedale Santa Maria della Misericordia	Udine
Domenico Amoroso	Ospedale Versilia	Lido di Camaiore

eTable 1. Main Demographic and Clinical Characteristics of Patients in the mITT Population

Characteristic	Arm A (n= 59)	Arm B (n= 57)	Overall mITT (n= 116)
Age (years)	61 (52-67)	59 (53-67)	59.5 (53-67)
Sex			
Male	40 (68%)	42 (74%)	82 (71%)
Female	19 (32%)	15 (26%)	34 (29%)
ECOG PS			
0	53 (90%)	50 (88%)	103 (89%)
1-2	6 (10%)	7 (12%)	13 (11%)
Synchronous Metastases			
Yes	51 (86%)	47 (82%)	98 (84%)
No	8 (14%)	10 (18%)	18 (16%)
Prior Adjuvant chemotherapy			
Yes	6 (10%)	8 (14%)	14 (12%)
No	53 (90%)	49 (86%)	102 (88%)
Primary Tumor Site			
Right	14 (24%)	7 (12%)	21 (18%)
Left	30 (51%)	35 (62%)	65 (56%)
Rectum	15 (25%)	15 (26%)	30 (26%)
Number of Metastatic Sites			
1	33 (56%)	29 (51%)	62 (53%)
>1	26 (44%)	28 (49%)	54 (47%)
Liver Only Disease			
Yes	28 (47%)	24 (42%)	52 (45%)
No	31 (53%)	33 (58%)	64 (55%)
Resected Primary Tumor			
Yes	35 (59%)	33 (58%)	68 (59%)
No	24 (41%)	24 (42%)	48 (41%)

Data are median (IQR) or number (%). ECOG PS, Eastern Cooperative Oncology Group Performance Status. Arm A indicates mFOLFOXIRI plus cetuximab, followed by maintenance with cetuximab. Arm B indicates mFOLFOXIRI plus cetuximab, followed by maintenance with bevacizumab.

eTable 2. Activity Results in the mITT Population

	Treatment arm		Overall population n= 116 No (%)
	Arm A (n= 59) No (%)	Arm B (n= 57) No (%)	
Complete response	3 (5%)	2 (3%)	5 (4%)
Partial response	37 (63%)	41 (72%)	78 (68%)
Stable disease	14 (24%)	8 (14%)	22 (19%)
Progressive disease	2 (3%)	2 (4%)	4 (3%)
Not evaluated	3 (5%)	4 (7%)	7 (6%)
Objective Response Rate	40 (68%)	43 (75%)	83 (72%)
Disease Control Rate	54 (92%)	51 (89%)	105 (91%)
	Arm A (n= 54) No (%)	**Arm B (n= 53) No (%)**	**Overall (n=107) No (%)**
Early Objective Response Rate	40 (74%)	41 (77%)	81 (76%)
Depth of Response, median (IQR)	49.1% (30.7%–67.9%)	55.7% (41.5%–67.6%)	53.2% (37.1%–67.6%)

Data are median (IQR) or number (%). Some percentages do not add up to 100 because of rounding. Arm A indicates mFOLFOXIRI plus cetuximab, followed by maintenance with cetuximab. Arm B indicates mFOLFOXIRI plus cetuximab, followed by maintenance with bevacizumab.

eTable 3. Grade ≥3 Adverse Events Occurring in at Least 3% of Patients During Induction and Maintenance

Safety results during induction			
AEs, No (%)	**Arm A (n= 59)**	**Arm B (n= 57)**	**Overall mITT n= 116**
Vomit	2 (3%)	1 (2%)	3 (3%)
Diarrhea	12 (20%)	9 (16%)	21 (18%)
Stomatitis	4 (7%)	3 (5%)	7 (6%)
Neutropenia	17 (29%)	19 (33%)	36 (31%)
Febrile neutropenia	2 (3%)	1 (2%)	3 (3%)
Neurotoxicity	4 (7%)	0	4 (3%)
Skin toxicity	11 (19%)	7 (12%)	18 (16%)
Asthenia	6 (10%)	5 (9%)	11 (9%)
Anorexia	3 (5%)	1 (2%)	4 (3%)
Venous thromboembolism	1 (2%)	2 (3%)	3 (3%)
Safety results during maintenance			
AEs, No (%)	**Arm A (n= 40)**	**Arm B (n= 38)**	**Maintenance population n= 78**
Hand-foot syndrome	2 (5%)	0	2 (3%)
Skin toxicity	8 (20%)	1 (3%)	9 (12%)
Hypertension	0	2 (5%)	2 (3%)

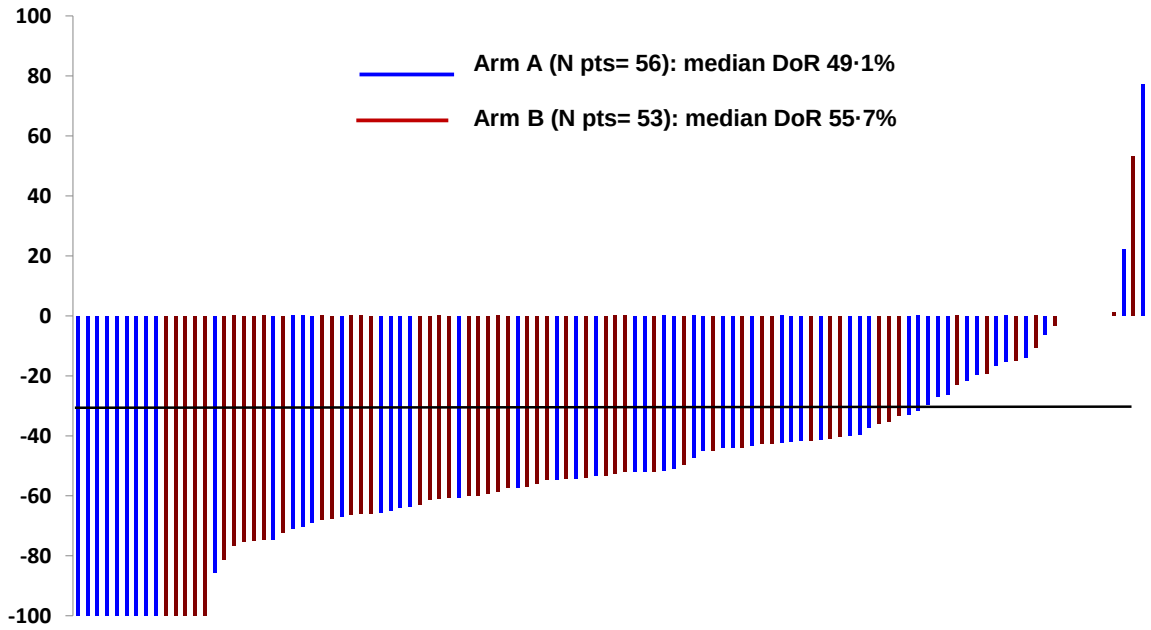
Data are number (%). AEs: adverse events. Arm A indicates mFOLFOXIRI plus cetuximab, followed by maintenance with cetuximab. Arm B indicates mFOLFOXIRI plus cetuximab, followed by maintenance with bevacizumab.

eTable 4. Treatments After Progression According to Randomization Arm

	Treatment arm		Overall mITT n= 116 No (%)
	Arm A (n= 59) No (%)	Arm B (n= 57) No (%)	
Alive after disease progression	53 (90%)	54 (95%)	107 (92%)
Any 2nd line therapy	43 (81%)	42 (78%)	85 (79%)
2nd line therapy	**n= 43**	**n= 42**	**n= 85**
mFOLFOXIRI plus cet	19 (44%)	28 (67%)	47 (55%)
FOLFOX/FOLFIRI plus cet	6 (14%)	7 (17%)	13 (15%)
FOLFOXIRI plus pan	2 (5%)	0	2 (2%)
cet or pan monotherapy	0	2 (5%)	2 (2%)
FOLFOXIRI plus bev	2 (5%)	0	2 (2%)
FOLFOX/FOLFIRI/XELOX plus bev	9 (21%)	2 (5%)	11 (13%)
capecitabine plus bev	2 (5%)	1 (2%)	3 (4%)
FOLFOX/FOLFIRI	3 (7%)	0	3 (4%)
Other	0	2 (5%)	2 (2%)

Data are number (%). Some percentages do not add up to 100 because of rounding. Cet: cetuximab; mFOLFOXIRI: modified fluorouracil, leucovorin, oxaliplatin and irinotecan; FOLFOX: fluorouracil, leucovorin, and oxaliplatin; FOLFIRI: fluorouracil, leucovorin, and irinotecan; bev: bevacizumab; pan: panitumumab; FOLFOXIRI: fluorouracil, leucovorin, oxaliplatin and irinotecan; XELOX: capecitabine and oxaliplatin. Arm A indicates mFOLFOXIRI plus cetuximab, followed by maintenance with cetuximab. Arm B indicates mFOLFOXIRI plus cetuximab, followed by maintenance with bevacizumab.

eFigure. Distribution of Deepness of Response in the mITT Population, According to Treatment Arm



DoR, depth of response; mos, months. Arm A indicates mFOLFOXIRI plus cetuximab, followed by maintenance with cetuximab. Arm B indicates mFOLFOXIRI plus cetuximab, followed by maintenance with bevacizumab.