

Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: FOxTROT Collaborative Group. Feasibility of preoperative chemotherapy for locally advanced, operable colon cancer: the pilot phase of a randomised controlled trial. *Lancet Oncol* 2012; published online Sept 25, 2012. [http://dx.doi.org/10.1016/S1470-2045\(12\)70348-0](http://dx.doi.org/10.1016/S1470-2045(12)70348-0).

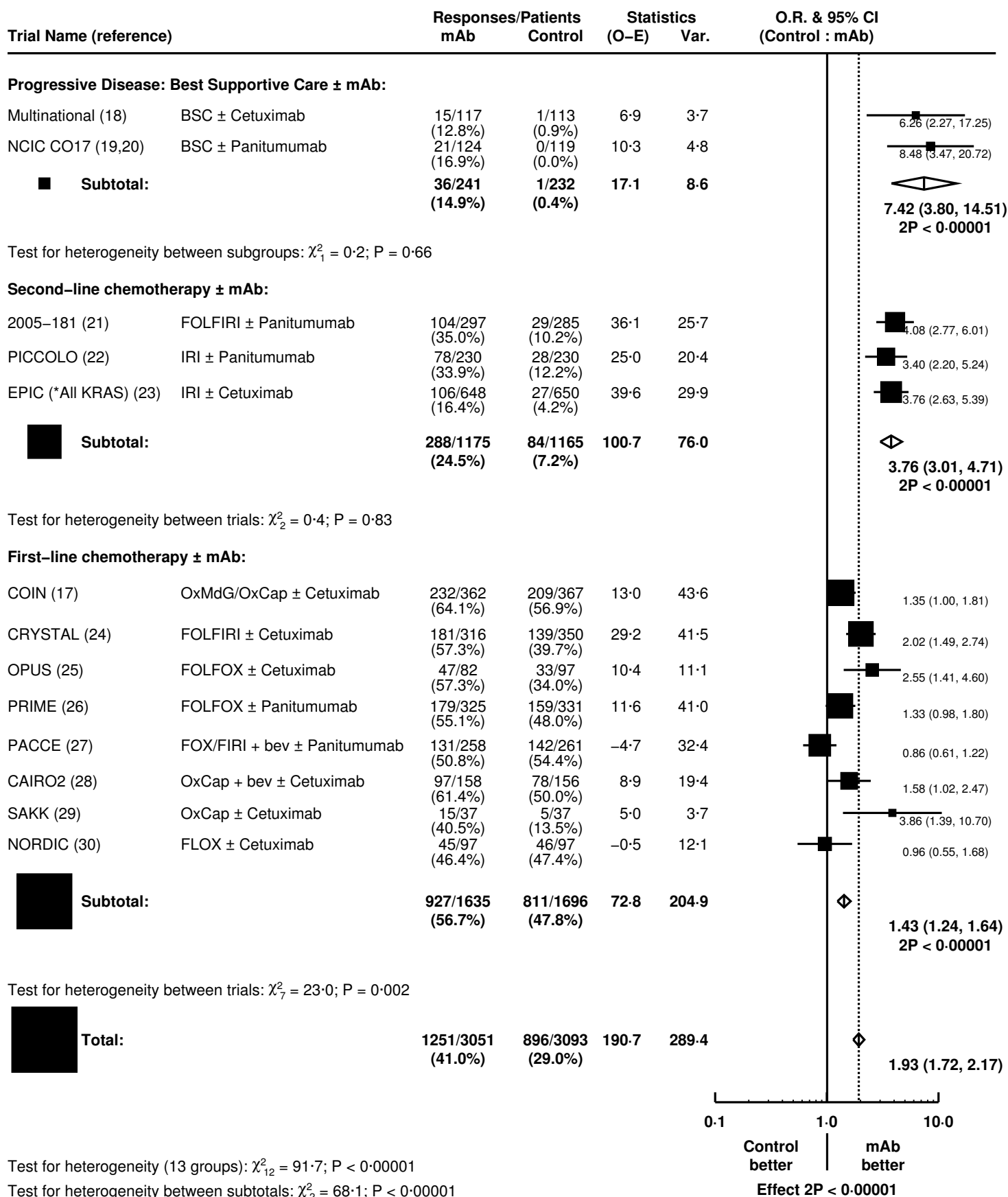
Appendix Table and Figures Legends

Appendix figure 1. Response rates in 13 trials of chemotherapy with or without EGFR-directed monoclonal antibody therapies in *K-RAS*-wildtype metastatic colorectal cancer stratified by previous chemotherapy exposure.

Appendix figure 2. KRAS-testing flow-chart

Appendix table 1. Toxicity experienced in each course of chemotherapy in the pre-plus post-operative chemotherapy group compared with the postoperative chemotherapy group

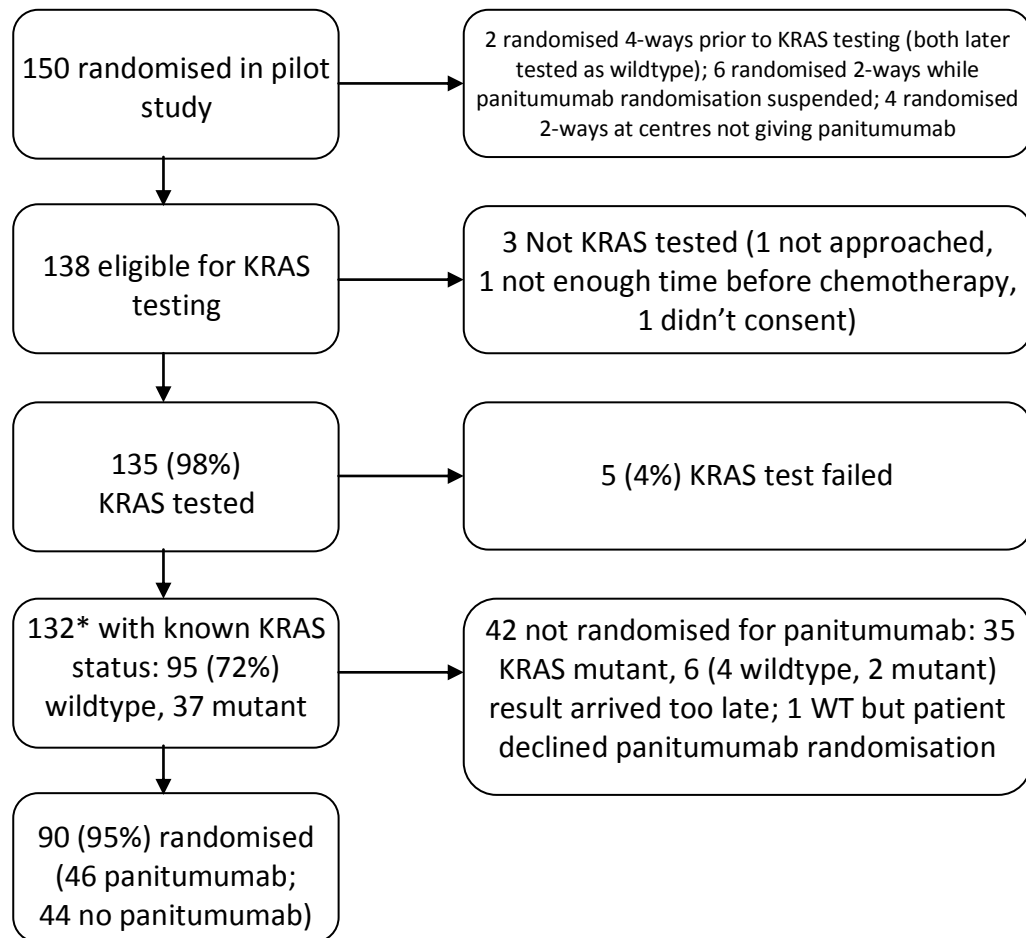
Appendix figure 1: Response rates in 13 trials of chemotherapy with or without EGFR-directed monoclonal antibody therapies in KRAS-wildtype* metastatic colorectal cancer stratified by previous chemotherapy exposure.



*KRAS-status was not available for EPIC study

Abbreviations: O.R.: Odds Ratio, O-E: Observed minus Expected numbers of events, Var: variance of O-E, BSC: Best Supportive Care, mAb: monoclonal antibody, bev: bevacizumab

Appendix figure 2. KRAS-testing flow-chart



* includes 2 randomised 4-ways prior to KRAS testing (both later tested as wildtype)

Appendix table 1. Toxicity experienced in each course of chemotherapy in the pre- plus post-operative chemotherapy group compared with the postoperative chemotherapy group

Patients starting course 1	Pre plus Post (n = 94[‡])		Post Only (n = 39)		p-value
Toxicity grade*:	Any grade	Grade 3+	Any grade	Grade 3+	any toxicity
Haematological	49 (52%)	19 (20%)	18 (46%)	5 (13%)	0.53
Platelets	11	-	3	-	0.49
Haemoglobin	36	-	8	-	0.05
WBC	20	8	6	-	0.44
Neutrophils	30	19	10	5	0.47
Skin	35 (37%)	7 (7%)	21 (54%)	3 (8%)	0.08
Alopecia	5	-	5	-	0.14
Nail changes	3	-	2	-	0.59
Skin rash	26	7	13	3	0.51
Hand/foot syndrome	7	-	7	-	0.07
Gastrointestinal	68 (72%)	7 (7%)	29 (74%)	4 (10%)	0.81
Anorexia	24	4	6	-	0.20
Diarrhoea	27	5	22	3	0.003
Stomatitis	38	-	10	1	0.11
Nausea	34	1	19	-	0.18
Vomiting	18	2	2	-	0.04
Pain	28 (30%)	5 (5%)	11 (28%)	2 (5%)	0.86
Pain	27	5	11	2	0.95
Vein pain	3	-	-	-	0.27
Lethargy	65 (69%)	6 (6%)	20 (51%)	1 (3%)	0.06
Peripheral neuropathy	47 (50%)	-	22 (56%)	-	0.50
Any category	90 (96%)	32 (34%)	36 (92%)	12 (31%)	0.42

*Toxicity grading used the Common Terminology Criteria for Adverse Events v3.0

[‡] One patient provided chemotherapy treatment information but did not complete a toxicity assessment

Patients starting course 2	Pre plus Post (n = 81)		Post Only (n = 38)		p-value any toxicity
	Any grade	Grade 3+	Any grade	Grade 3+	
Haematological	41 (51%)	9 (11%)	21 (55%)	4 (11%)	0.64
Platelets	17	-	11	-	0.34
Haemoglobin	26	2	10	-	0.52
WBC	15	2	8	-	0.75
Neutrophils	20	7	13	4	0.28
Skin	26 (32%)	-	15 (39%)	2 (5%)	0.43
Alopecia	10	-	9	-	0.11
Nail changes	2	-	5	-	0.02
Skin rash	8	-	7	2	0.19
Hand/foot syndrome	9	-	2	-	0.31
Gastrointestinal	49 (60%)	5 (6%)	31 (82%)	2 (5%)	0.02
Anorexia	12	1	6	-	0.89
Diarrhoea	35	3	20	1	0.34
Stomatitis	48	4	24	-	0.69
Nausea	24	1	14	-	0.43
Vomiting	4	-	2	-	0.94
Pain	22 (27%)	1 (1%)	10 (26%)	-	0.92
Pain	21	1	8	-	0.57
Vein pain	1	-	2	-	0.19
Lethargy	48 (59%)	4 (5%)	24 (63%)	-	0.69
Peripheral neuropathy	55 (68%)	1 (1%)	29 (76%)	2 (5%)	0.35
Any category	77 (95%)	14 (17%)	37 (97%)	9 (24%)	0.56

Patients starting course 3	Pre plus Post (n = 75)		Post Only (n = 34)		p-value any toxicity
	Any grade	Grade 3+	Any grade	Grade 3+	
Haematological	42 (56%)	6 (8%)	20 (59%)	4 (12%)	0.78
Platelets	27	1	8	-	0.20
Haemoglobin	26	1	8	-	0.25
WBC	11	1	6	-	0.69
Neutrophils	23	6	15	4	0.17
Skin	25 (33%)	1 (1%)	9 (26%)	-	0.48
Alopecia	10	-	5	-	0.85
Nail changes	5	-	3	-	0.69
Skin rash	4	-	3	-	0.49
Hand/foot syndrome	15	1	2	-	0.06
Gastrointestinal	48 (64%)	7 (9%)	23 (68%)	2 (6%)	0.71
Anorexia	9	-	6	-	0.43
Diarrhoea	30	6	18	1	0.21
Stomatitis	25	2	11	1	0.92
Nausea	24	1	11	-	0.97
Vomiting	3	-	3	-	0.31
Pain	17 (23%)	1 (1%)	2 (6%)	1 (3%)	0.03
Pain	17	1	2	1	0.03
Vein pain	-	-	-	-	
Lethargy	50 (67%)	3 (4%)	21 (62%)	2 (6%)	0.62
Peripheral neuropathy	48 (64%)	2 (3%)	30 (88%)	1 (3%)	0.01
Any category	74 (99%)	18 (24%)	33 (97%)	8 (24%)	0.56

Patients starting course 4	Pre plus Post (n = 73)		Post Only (n = 31)		p-value any toxicity
	Any grade	Grade 3+	Any grade	Grade 3+	
Haematological	39 (53%)	5 (7%)	9 (29%)	3 (10%)	0.02
Platelets	26	1	5	1	0.05
Haemoglobin	22	-	4	-	0.07
WBC	15	-	2	-	0.08
Neutrophils	22	4	5	2	0.14
Skin	21 (29%)	-	10 (32%)	-	0.72
Alopecia	8	-	4	-	0.78
Nail changes	8	-	3	-	0.85
Skin rash	7	-	1	-	0.27
Hand/foot syndrome	10	-	5	-	0.75
Gastrointestinal	37 (51%)	2 (3%)	14 (45%)	1 (3%)	0.61
Anorexia	8	-	1	-	0.20
Diarrhoea	18	2	9	1	0.64
Stomatitis	18	-	8	-	0.90
Nausea	15	-	4	-	0.36
Vomiting	1	-	1	-	0.53
Pain	8 (11%)	-	4 (13%)	-	0.78
Pain	8	-	4	-	0.78
Vein pain	-	-	-	-	
Lethargy	43 (59%)	3 (4%)	12 (39%)	-	0.06
Peripheral neuropathy	38 (52%)	-	24 (77%)	3 (10%)	0.02
Any category	66 (90%)	9 (12%)	28 (90%)	7 (23%)	0.99

Over all courses	Pre plus Post (n = 95)		Post Only (n = 39)		p-value any toxicity
	Any grade	Grade 3+	Any grade	Grade 3+	
Haematological	71 (75%)	28 (29%)	25 (64%)	11 (28%)	0.22
Platelets	41	2	12	1	0.18
Haemoglobin	51	2	13	-	0.03
WBC	38	8	11	-	0.20
Neutrophils	51	28	21	10	0.99
Skin	56 (59%)	8 (8%)	27 (69%)	3 (8%)	0.27
Alopecia	15	-	9	-	0.32
Nail changes	10	-	6	-	0.43
Skin rash	32	7	15	3	0.60
Hand/foot syndrome	22	1	11	-	0.54
Gastrointestinal	82 (86%)	18 (19%)	35 (90%)	8 (21%)	0.59
Anorexia	38	5	10	-	0.12
Diarrhoea	54	14	31	5	0.01
Stomatitis	52	2	23	3	0.66
Nausea	56	3	23	-	1.00
Vomiting	24	2	5	-	0.11
Pain	45 (47%)	6 (6%)	18 (46%)	2 (5%)	0.90
Pain	44	6	18	2	0.99
Vein pain	3	-	2	-	0.59
Lethargy	85 (89%)	13 (14%)	31 (79%)	3 (8%)	0.13
Peripheral neuropathy	77 (81%)	2 (2%)	37 (95%)	5 (13%)	0.04
Any category	94 (99%)	47 (49%)	39 (100%)	20 (51%)	0.96