

Table S1. Most relevant studies addressing the management of primary tumor in patients with metastatic colorectal cancer

Study	Study type	Enrollment interval	Patients		Rectal cancer (% of all patients)	Median overall survival (months)			Chemotherapy regimens
			Resection group (N)	Non-resection group (N)		Resection group	Non-resection group	P value	
Xu et al.	Retrospective, large database	1988-2010	27931	16583	34	16	7	HR 0.45 (0.44-0.46)	CT regimen not specified
Konyalian et al.	Retrospective, single center	1991-2002	62	47	26	12.5	4.6	<0.001	NR
Ahmed et al.	Retrospective cohort study	1992-2005	944	434	30	Resection of PT + CT: 18.3	Only CT: 8.4	<0.0001	5-FU-based chemotherapy
Ahmed et al.	Retrospective	1992-2005	521	313	33	19.7 29.4	8.4 16.0	<0.0001 <0.001	5-FU-LV Oxaliplatin- or irinotecan-based
Beham et al.	Retrospective, single center	1993-2003	46	21	43	18.1	7.8	<0.001	CT regimen not specified
Duraker et al.	Prospective cohort study	1993-2004	110	54	46	11.0	5.5	<0.001	5-FU-based
Costi et al.	Retrospective, single center	1994-2003	83	47	21	9	4	<0.001	No CT.
Stelzner et al.	Retrospective, single center	1995-2001	82	25	39	11.7	5.2	0.0002 (univariate)	5-FU-based
Galizia et al.	Retrospective, single center	1995-2005	42	23	18	15.2	12.3	0.03	5-FU-based/Oxaliplatin/Irinotecan
Ruo et al.	Retrospective, single center	1996-1999	127	103	32	16.0	9.0	<0.001	CT regimen not specified Radiation
Mik et al.	Retrospective, single center	1996-2000	52	82	48	21	14	0.004	5-FU-LV
Tsang et al.	Retrospective, large database	1996-2007	8599	3117	20	21	10	<0.0001	CT regimen not specified
Ferrand et al.	Post-hoc analysis of a multicenter RT	1997-2001	156	60	20	16.3	9.5	<0.0001	5-FU-LV ± Raltitrexed
Ishihara et al.	Retrospective, multicenter	1997-2007	1782	200	23	17.2 (CSS)	6.4 (CSS)	<0.01	CT regimen not specified
Faron et al.	Pooled analysis of individual data from four RT	1997-2008	478	332	18	19.2	13.3	<0.001	5-FU-LV/Raltitrexed/FOLFOX/ FOLFIRI ± bevacizumab/ XELIRI + bevacizumab/
Kaufman et al.	Retrospective, single center	1998-2003	115	69	28	22.0 (surgery) 30.0 (surgery + CT)	3.0 (no CT) 15.0 (CT)	<0.0001 <0.00041	CT regimen not specified
Aslam et al.	Retrospective, single center	1998-2007	366	281	35	14.5	5.8	<0.001	CT regimen not specified
Karoui et al.	Retrospective, multicenter	1998-2007	85	123	0	30.7	21.9	0.031	Oxaliplatin-or irinotecan-containing ± anti-VEGFR/anti-EGFR drug
Tarantino et al.	Retrospective, large database	1998-2009	23004	14789	19	NR	NR	HR 0.40 P<0.001	CT regimen not specified

Bajwa et al.	Retrospective, single center	1999-2005	32	35	NR	14.0	6.0	0.005	5-FU-based/Oxaliplatin/Irinotecan
Chan et al.	Retrospective, population-based cohort	2000-2002	286	125	24	14.0	6.0	<0.001	5-FU Irinotecan
Yoon et al.	Prospective cohort study, single center	2000-2007	195	66	42	21	10	<0.001	FOLFOX/FOLFIRI/XELOX/XELIRI/ 5-FU-LV/capecitabine ± bevacizumab, cetuximab
Park et al.	Retrospective, single center	2000-2009	527	320	NR	21.4	14.1	<0.001	Oxaliplatin/Irinotecan/capecitabine ± bevacizumab/cetuximab
Ahn et al.	Retrospective, single center	2001-2009	28	36	25	12.43	3.58	<0.001	5-FU-LV/FOLFOX/FOLFIRI
Venderbosch et al.	Retrospective analysis of two RT	2003-2004 2005-2006	258 289	141 159	26 19	16.7 20.7	11.4 13.4	<0.0001 <0.0001	Capecitabine + Oxaliplatin + Irinotecan Capecitabine + Oxaliplatin+ Bevacizumab ± Cetuximab
Gulack et al.	Retrospective, large database	2003-2006	231	1215	40	9.2	7.6	<0.01	CT regimen not specified
Tanoue et al.	Retrospective, single center	2005-2009	38	36	47	30.6	20.8	0.0094	FOLFOX/FOLFIRI ± bevacizumab/cetuximab
Ichikawa et al.	Retrospective, single center	2005-2010	37	58	NR	30.7	21.9	0.031	CT regimen not specified
Gresham et al.	Retrospective, multicenter	2006-2008	378	139	24	17.9	7.9	<0.0001	FOLFOX/FOLFIRI ± bevacizumab/ capecitabine/5FU
Ahmed et al.	Retrospective, single center	2006-2010	313	256	33	Resection of PT + CT: 27	Only CT: 14	<0.001	FOLFOX/FOLFIRI ± bevacizumab/ cetuximab/panitumumab
Kim et al.	Retrospective, single center	2006-2010	72	252	30	17.2	13.6	0.002	Oxaliplatin-based or irinotecan-based ± anti-VEGF/anti-EGFR
't Lam-Boer et al.	Retrospective, large database	2008-2011	2746	3345	23	17.2	11.5	<0.001	CT regimen not specified
Wong et al.	Retrospective, large database	2009-2015	216	394	24	21	17	0.014	CT regimen not specified ± bevacizumab/cetuximab
Wang et al.	Prospective cohort study, single center	2011-2013	118	73	40	22.5	17.8	<0.01	FOLFOX/XELOX/FOLFIRI + bevacizumab

5-FU: 5-fluorouracil; BSC: best supportive care; CSS: cancer-specific survival; CT: chemotherapy; HR: hazard ratio; LV: leucovorin; PT: primary tumor; RT: randomized trial.

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