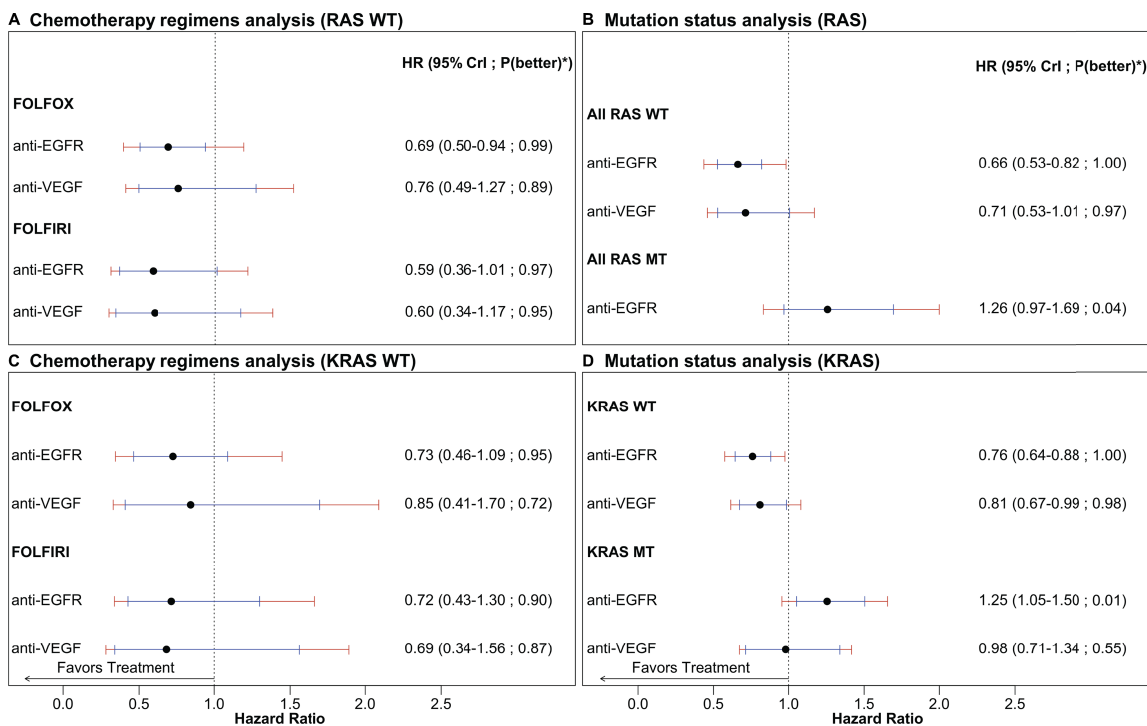
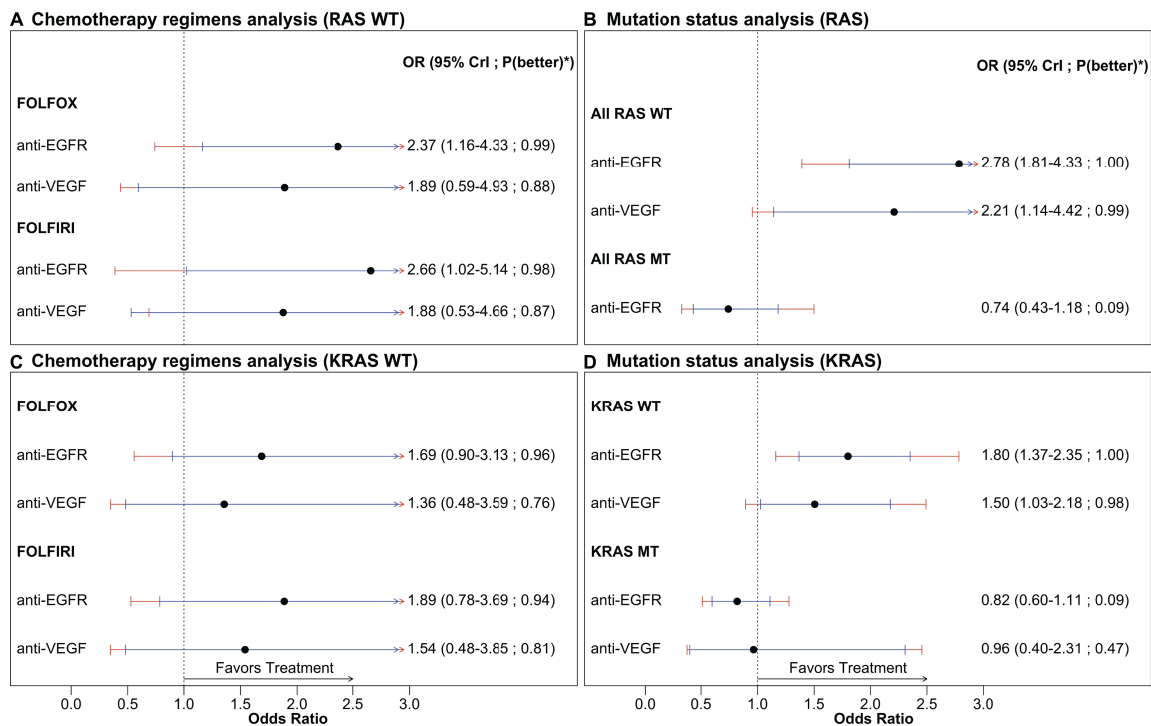


Targeted first-line therapies for advanced colorectal cancer: a Bayesian meta-analysis

SUPPLEMENTARY MATERIALS



Supplementary Figure 1: PFS comparisons of anti-EGFR and anti-VEGF therapies as first-line treatment for advanced or metastatic colorectal cancer. (A) and (C) Chemotherapy regimen comparison for *all-RAS* and *KRAS* WT. (B) and (D) Mutation status comparison for *all-RAS* and *KRAS*. Treatments are compared to chemotherapy alone. Bayesian network estimates reported as hazard ratio (95% credible intervals in black and 95% predictive intervals in red). *Probability that the treatment arm is better than chemotherapy alone.



Supplementary Figure 2: ORR comparisons of anti-EGFR and anti-VEGF therapies as first-line treatment for advanced or metastatic colorectal cancer. (A) and (C) Chemotherapy regimen comparison for *all-RAS* and *KRAS* WT. (B) and (D) Mutation status comparison for *all-RAS* and *KRAS*. Treatments are compared to chemotherapy alone. Bayesian network estimates reported as odds ratio (95% credible intervals in black and 95% predictive intervals in red). *Probability that the treatment arm is better than chemotherapy alone.

Supplementary Table 1: Characteristics of studies included for meta-analysis for the secondary endpoint progression-free survival including patient population, treatment arms, and effect estimates (HRs) for subgroups defined by *KRAS*, all-*RAS*, or *BRAF* mutation status

Trial	Treatments (N)	All- <i>RAS</i> WT	Any <i>RAS</i> MT	<i>KRAS</i> WT	<i>KRAS</i> MT	<i>BRAF</i> ^c WT	<i>BRAF</i> ^c MT
CRYSTAL ^{1,2}	FOLFIRI + cetuximab (599)	0.56 (0.41–0.76)	1.1 (0.85–1.42)	0.70 (0.56–0.87)	1.17 (0.89–1.54)	0.53 (0.37–0.75)	–
	FOLFIRI ^a (599)						
OPUS ^{3,4}	FOLFOX + cetuximab (169)	0.53 (0.27–1.04)	1.54 (1.04–2.29)	0.57 (0.38–0.86)	1.72 (1.10–2.68)	0.51 (0.25–1.05)	–
	FOLFOX ^a (168)						
FIRE-3 ^{5,6}	FOLFIRI + cetuximab (297)	0.97 (0.78–1.20)	–	1.06 (0.88–1.26)	–	–	–
	FOLFIRI + bevacizumab ^b (295)						
PEAK ⁷	FOLFOX + panitumumab (142)	0.65 (0.44–0.96)	–	0.87 (0.65–1.17)	–	–	–
	FOLFOX + bevacizumab ^b (143)						
PRIME ^{8,9}	FOLFOX + panitumumab (546)	0.72 (0.58–0.9)	1.31 (1.07–1.6)	0.8 (0.67–0.95)	1.27 (1.04–1.55)	0.68 (0.54–0.87)	0.58 (0.29–1.15)
	FOLFOX ^a (550)						
CECOG/ CORE1.2.001 ¹⁰	FOLFOX + cetuximab (77)	–	–	0.49 ^d (0.27–0.91)		–	–
	FOLFIRI+ cetuximab (74)			0.66 ^d (0.36–1.21)			
AIO KRK 0306 ¹¹	FOLFIRI + cetuximab (50)	–	–	–	1.00 (0.66–1.53)	–	–
	FOLFIRI + bevacizumab ^b (46)						
CALGB-SWOG 80405 ¹²	Chemotherapy ^b + cetuximab (578)	1.03 ^c (0.86–1.24)	–	0.95 (0.84–1.08)	–	–	–
	Chemotherapy ^b + bevacizumab ^a (559)						
ITACa ¹³	Chemotherapy ^b + bevacizumab (176)	–	–	0.95 (0.73–1.24)	0.83 (0.58–1.18)	–	–
	Chemotherapy ^{a,b} (194)						
TAILOR ¹⁴	FOLFOX + cetuximab (193)	0.69 (0.54–0.89)	–	–	–	–	–
	FOLFOX ^c (200)						

^aReference arm; ^bFOLFOX or FOLFIRI; ^c*BRAF* evaluated within *RAS* WT subgroup; ^dThe reported HR is for WT compared to MT for each arm; ^eFor FOLFOX and FOLFIRI, the respective HRs are 1.1 (95% CI 0.9–1.4) and 1.1 (95% CI 0.7–1.5).

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Supplementary Table 2: Characteristics of studies included for meta-analysis for the secondary endpoint overall response rate including patient population, treatment arms, and effect estimates (ORs) for subgroups defined by KRAS, all-RAS, or BRAF mutation status

Trial	Treatments (N)	All-RAS WT	Any RAS MT	KRAS WT	KRAS MT	BRAF ^c WT	BRAF ^c MT
CRYSTAL ^{1,2}	FOLFIRI + cetuximab (599)	3.11 (2.03–4.78)	0.85 (0.58–1.25)	2.07 (1.52–2.83)	0.82 (0.54–1.24)	3.29 (2.06–5.26)	–
	FOLFIRI ^a (599)						
OPUS ^{3,4}	FOLFOX + cetuximab (169)	3.33 (1.36–8.17)	0.58 (0.31–1.08)	2.55 (1.38–4.72)	0.46 (0.23–0.92)	3.44 (1.34–8.82)	–
	FOLFOX ^a (168)						
FIRE-3 ^{5,6}	FOLFIRI + cetuximab (297)	1.33 (0.88–1.99)	–	1.18 (0.85–1.64)	–	–	–
	FOLFIRI + bevacizumab ^b (295)						
PEAK ⁷	FOLFOX + panitumumab (142)	1.14 (0.61–2.11)	–	1.2 (0.75–1.92)	–	–	–
	FOLFOX + bevacizumab ^b (143)						
PRIME ^{8,9}	FOLFOX + panitumumab (546)	–	–	1.47 (1.07–2.04)	0.98 (0.65–1.47)	–	–
	FOLFOX ^a (550)						
CECOG/ CORE1.2.001 ¹⁰	FOLFOX + cetuximab (77)	–	–	2.90 ^d (0.95–8.84)		–	–
	FOLFIRI + cetuximab (74)			1.46 ^d (0.53–4.07)			
AIO KRK 0306 ¹¹	FOLFIRI + cetuximab (50)	–	–	–	0.85 (0.37–1.98)	–	–
	FOLFIRI + bevacizumab ^b (46)						
CALGB-SWOG 80405 ¹²	Chemotherapy ^b + cetuximab (578)	–	–	1.20 (0.95–1.52)	–	–	–
	Chemotherapy ^b + bevacizumab ^b (559)						
TAILOR ¹³	FOLFOX + cetuximab (193)	2.41 (1.61–3.61)	–	–	–	–	–
	FOLFOX ^a (200)						

^aReference arm; ^bFOLFOX or FOLFIRI; ^cBRAF evaluated within RAS WT subgroup; ^dThe reported OR is for WT compared to MT for each arm; ^eThe reported OR is for MT compared to WT.

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