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**Treatment Effect of Panitumumab versus Best Supportive Care (BSC)
in Patients With Metastatic Colorectal Cancer (mCRC): Results of
Sensitivity Analyses From a Phase III Randomized Controlled Trial**

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Background: Panitumumab is a fully human monoclonal antibody directed against the epidermal growth factor receptor (EGFR) and significantly improved progression-free survival (PFS) vs BSC in this phase III trial (Peeters AACR 2006; Van Cutsem WCGIC 2006). Prespecified sensitivity analyses were conducted to further evaluate the treatment effect of panitumumab.

Methods: Patients had mCRC, Eastern Cooperative Oncology Group (ECOG) performance status 0-2, radiologic disease progression (PD) during or within 6 months of most recent chemotherapy (fluoropyrimidine, irinotecan, and oxaliplatin), and $\geq 1\%$ EGFR tumor cell membrane staining by immunohistochemistry. Patients were randomized 1:1 to receive panitumumab 6 mg/kg every 2 weeks + BSC or BSC alone. Tumor assessments (modified Response Evaluation Criteria in Solid Tumors [RECIST], blinded central review) were scheduled from week 8 until PD. BSC patients could receive panitumumab in a crossover study after investigator assessment of PD. Prespecified sensitivity analyses of PFS included main study events only, central

adjudication of prior chemotherapy exposure, and investigator assessment. Secondary endpoints included objective response rates (ORR) and safety.

Results: A total of 463 patients (231 panitumumab, 232 BSC) were randomized. The groups were well balanced at baseline: all but 1 received ≥ 2 prior chemotherapy regimens; 75% had ≥ 2 metastatic sites. PFS favored panitumumab (HR: 0.54 [95% CI:0.44, 0.66]). In all sensitivity analyses, PFS favored panitumumab and was consistent with that of the primary analysis (Table). ORR favored panitumumab vs BSC: partial response, 8% vs 0% ($P < .0001$); stable disease, 28% vs 10%, respectively. Panitumumab was well tolerated.

Conclusions: In all sensitivity analyses, panitumumab improved PFS vs BSC and was well tolerated in mCRC patients who failed standard chemotherapy.

Hazard Ratios^a (95% CI) for PFS by Prespecified Sensitivity Analyses

	Central Radiology				Local Radiology
	All events	Events in main study	Skipped Assessments ^b	Interval censored ^c	
All Randomized (n = 463 [100%])	0.54 (0.44, 0.66)	0.41 (0.33, 0.51)	0.56 (0.45, 0.68)	0.61 (0.49, 0.75)	0.39 (0.32, 0.48)
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Prior Failures (n = 352 [76%])	0.59 (0.47, 0.75)	0.45 (0.35, 0.58)	0.60 (0.48, 0.75)		0.42 (0.33, 0.53)
Per Protocol (n = 337 [73%])	0.63 (0.50, 0.80)				0.41 (0.32, 0.52)

^aAdjusted for ECOG performance status and geographic region; hazard ratios presented as panitumumab:BSC.

^bIf disease progression or death in the panitumumab group occurred after ≥ 2 consecutive skipped visits, the event was moved to the first missed visit.

^cPost-hoc analysis; Interval censored analysis imputed radiographic disease progression to the nearest scheduled tumor assessment.

All P -values were $< .0001$