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A VELOUR POST HOC SUBSET ANALYSIS: PROGNOSTIC GROUPS AND TREATMENT OUTCOMES IN PATIENTS WITH METASTATIC COLORECTAL CANCER (MCRC) TREATED WITH AFLIBERCEPT AND FOLFIRI

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Background: The VELOUR study demonstrated a significant survival benefit for aflibercept (ziv-aflibercept in the USA) plus FOLFIRI (5-fluorouracil-leucovorin-irinotecan) versus placebo plus FOLFIRI in patients with metastatic colorectal cancer that is resistant to or has progressed after an oxaliplatin-containing regimen. Adding aflibercept to FOLFIRI gave an overall median survival relative to placebo plus FOLFIRI of 13.50 versus 12.06 months (OS hazard ratio [HR], 0.817; 95% CI: 0.713–0.937; *P* = .0032) and a median progression-free survival of 6.90 versus 4.67 months (PFS HR, 0.758; 95% CI: 0.661–0.869; *P* = .00007), respectively. The response rate in VELOUR was 19.8% (95% CI, 16.4%–23.2%) for aflibercept plus FOLFIRI and 11.1% (95% CI, 8.5%–13.8%) for placebo plus FOLFIRI (*P* = .0001). Kaplan-Meier analysis of the intent-to-treat population showed a continued divergence of survival curves, with persistence of the survival effect lasting beyond the median survival time. This result suggests that there may be subsets of patients who derive sustained survival benefit with the combination of aflibercept and FOLFIRI. The objective of this study was to identify a better responder subgroup in the VELOUR population.

Methods: Pre-specified multivariate analysis (covariates: demographics, Eastern Cooperative Oncology Group [ECOG] performance status [PS], prior bevacizumab status, age, prior hypertension, and number of metastatic organs involved) identified a subset of patients with better outcomes on the aflibercept and FOLFIRI combination. This subset of "better responders" was identified as patients with PS0; PS1 and ≤1 metastatic site in patients who did not experience an early relapse (ie, had recurrence during or within 6 months of completing adjuvant oxaliplatin-based therapy [adjuvant-only]). This population included 404/612 aflibercept and FOLFIRI patients and 406/614 placebo and FOLFIRI patients.

Results: In the "better responders" subset, median overall survival was significantly improved in the aflibercept arm: 16.2 versus 13.1 months for placebo (adjusted HR=0.73 [95% CI: 0.61-0.86]). Median progression-free survival was significantly improved with aflibercept: 7.2 versus 4.8 months for placebo (adjusted HR=0.68 [95% CI: 0.57-0.80]). Complete or partial response occurred in 23.7% (84/354) of aflibercept versus 11% (39/354) of placebo patients.

Conclusions: Post hoc analysis suggested that the "better responders" subgroup of patients within VELOUR derived an enhanced efficacy benefit with the aflibercept and FOLFIRI combination, with more than 2-fold increase in overall survival gains (3.1 months) compared with the ITT population. These results may help optimize clinical management reimbursement decision support in mCRC.

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