Quality-of-life results from RAISE: randomized, double-blind phase III study of FOLFIRI plus ramucirumab or placebo in patients with metastatic colorectal carcinoma after first-line therapy with bevacizumab, oxaliplatin, and a fluoropyrimidine


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Introduction: The RAISE trial demonstrated a statistically significant overall and progression-free survival benefit for the addition of ramucirumab to FOLFIRI as second-line therapy for patients with metastatic colorectal carcinoma failing first-line oxaliplatin-based chemotherapy with bevacizumab, along with a manageable safety profile. We present the secondary endpoint of quality of life (QoL).

Methods: Eligible patients had progressed on or after first-line therapy of bevacizumab, oxaliplatin, and a fluoropyrimidine. Patients were randomized to receive ramucirumab 8 mg/kg plus FOLFIRI or placebo plus FOLFIRI every 2 weeks. Patients completed the EORTC QLQ-C30 (version 3) at baseline, prior to every other cycle for the first 6 months, then prior to every fourth cycle, at treatment discontinuation, and at 30-day follow-up. For each of the 15 QoL scales and at each postbaseline assessment, patients were classified as improved or worsened if change from baseline was greater than or equal to 10 points (100-point scale); changes <10 points were considered stable. Rates of improved/stable scores were compared with a chi-square test. Time to deterioration (TtD) in QoL was defined as time elapsed from the randomization date to the first worsened change from baseline score of greater than or equal to 10 points. Post hoc analysis of time to sustained deterioration (TtSD) was defined as time elapsed from the randomization date to the first worsened score without a subsequent nonworsened score. TtD and TtSD were analyzed with a stratified log-rank test with hazard ratios <1 favoring ramucirumab plus FOLFIRI. All analyses were based on the intention-to-treat (ITT) population, and p < 0.05 was considered statistically significant with no adjustments for multiplicity.

Results: A total of 1072 patients (n = 536 per arm) were randomized and comprised the ITT population. Patients in both arms received a median of 8 cycles of study treatment. In both arms, 91% of patients provided both a baseline and at least one postbaseline QoL assessment. Baseline scores were similar between arms. Rates of improved/stable scores were not statistically different between arms except for lower rates in the ramucirumab plus FOLFIRI arm before Cycle 3 for global QoL, physical functioning, role functioning, cognitive functioning, social functioning, pain, and dyspnea, and before Cycles 3 and 5 for fatigue and appetite loss. No differences in rates of improved/stable scores were observed for subsequent assessments. Further exploration of data suggested Cycle 3 worsening was not directly associated with discontinuation of therapy. For TtD, hazard ratios were >1 with p < 0.05 for global QoL, physical functioning, role functioning, emotional functioning, fatigue, appetite loss, and constipation. For TtSD, hazard ratios were >1 with p < 0.05 for emotional functioning, fatigue, and appetite loss. All other TtD and TtSD analyses had p value greater than or equal to 0.05.

Conclusion: Consideration of all analyses suggested a transient worsening of QoL for the ramucirumab plus FOLFIRI arm relative to the placebo plus FOLFIRI arm. When assessing for sustained deterioration, no statistical differences were observed in the majority of the QoL scales. The addition of ramucirumab to FOLFIRI extends overall and progression-free survival without sustained impairment in most dimensions of QoL.