Colon Cancer Mutation: Prognosis/Prediction–Letter

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We read with great interest the recent study by Gavin and colleagues (1), who evaluated the prognostic and predictive value of DNA mismatch repair (MMR) status for oxaliplatin-containing adjuvant chemotherapy in patients with stage II and III colon cancer from National Surgical Adjuvant Breast and Bowel Project clinical trials C-07 and C-08. Of note, C-07 showed that the addition of oxaliplatin to 5-fluorouracil (5-FU) and leucovorin significantly improved disease-free-survival (DFS) but not overall survival (OS), and C-08 found no benefit for the addition of bevacizumab to FOLFOX as adjuvant chemotherapy.

Increasing evidence indicates that deficient MMR (dMMR) status is a biomarker of good prognosis, and that it can predict the lack of efficacy of adjuvant 5-FU (2). Therefore, some authors recommend that patients with stage II dMMR colon cancer should not receive 5-FU, whereas there is no consensus regarding the treatment of dMMR stage III colon cancer (2). This issue is complicated by the fact that FOLFOX is the current standard regimen for stage III colon cancer, and preclinical data indicate that MMR-deficient tumor cells are sensitive to oxaliplatin (3) despite displaying resistance to 5-FU. A preliminary clinical study suggested that the addition of oxaliplatin may reverse the 5-FU resistance for dMMR stage III colon cancer (4). However, no data are provided as yet by randomized and controlled clinical trials. In the recent study of Gavin and colleagues (1), the authors show that dMMR was a favorable prognostic marker for OS and was associated with delayed time-to-recurrence (TTR). MMR status was not predictive of oxaliplatin efficacy, as the interaction test between MMR status and treatment was not statistically significant. Accordingly, we can assume that any benefit induced by oxaliplatin is similar in dMMR and proficient MMR patients. However, additional data would be of great interest for the clinicians, as it may help to better understand the complex impact of MMR status on adjuvant treatment in patients with colon cancer. Specifically, we request TTR, DFS, and OS Kaplan–Meier curves comparing 5-FU and leucovorin with or without oxaliplatin plotted according to MMR status within C-07, and by MMR status for FOLFOX treatment using pooled data from C-07 and C-08 trials. Another issue to be addressed in future studies will be to evaluate the benefit of oxaliplatin according to the mechanism of MMR deficiency, as a different response to 5-FU has been described for sporadic versus germline dMMR cases (5).

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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References


