Challenges of Efficacy Assessments in Pseudomyxoma Peritonea

Several critical issues need to be considered in interpreting the results of the single-center observational study of the FOLFOX regimen in appendiceal pseudomyxoma peritonei (PMP) reported by Pietrantonio et al. [1].

Clinical behavior of mucinous appendiceal neoplasms is variable and highly dependent on histological grade [2]. Currently, multiple histopathological grading systems exist [3–5]. Although the authors' eligibility criteria describe inclusion of borderline mucinous tumors and well-differentiated appendiceal adenocarcinomas, the grading is reported as either low ($n = 12$) or high ($n = 8$). Because no reference grading system is provided, the meaning of high and low grade is unclear. According to the American Joint Committee on Cancer's AJCC Cancer Staging Manual, 7th edition, high-grade mucinous appendiceal adenocarcinomas are defined as moderate to poorly differentiated tumors [6], and that is inconsistent with the inclusion criteria.

Eligible patients were either unresectable ($n = 6$) or had relapsed following initial cytoreductive surgery (CRS; $n = 14$). It was reported that 2 of the 6 initially unresectable cases underwent cytoreductive surgery, but the rate of repeat CRS in the 14 patients who had initially relapsed following a complete CRS was not reported. Because repeated CRS in appendiceal PMP represents a proven approach [7, 8] the rate of a second CRS should be reported. Because both PFS and overall survival times are not censored at the time of a second CRS, the reported time-to-event analyses may best reflect an anticancer approach of chemotherapy followed by repeated CRS [9].

Low-grade mucinous appendiceal neoplasms are known to have an indolent disease course; therefore, the presence of 7 cases with $>20\%$ growth at 3 months (progressive disease) is highly unusual for this disease type. Furthermore, the $>30\%$ shrinkage seen in 4 of these patients is unusual in the context of a median of 8 cycles (~ 4 months) and a maximum of 12 (~ 6 months). As a center that has conducted extensive research in appendiceal neoplasms, we disagree with the statement that a "decrease in the amount of mucus was invariably observed" and feel that the magnitude of radiographic change reported over a 3- to 6-month period for low-grade mucinous appendiceal neoplasms is not an accurate reflection of the disease biology under study. Prior reports documenting radiographic responses have all included more aggressive and higher grade appendiceal neoplasms and are not reflective of the population in this report [10, 11]. In part, we believe that the findings reported reflect the intrinsic challenges of both separating mucinous from more serous peritoneal accumulations and measuring geographically shaped mucinous implants that shift between scans. This latter point is amplified by the limitation of measuring only two peritoneal areas, as

per Response Evaluation Criteria In Solid Tumors (RECIST) version 1.1.

Prospective controlled studies are needed to clarify the role of chemotherapy in PMP. A clinical trial (NCT01946854) for unresectable low-grade mucinous appendiceal adenocarcinomas with PMP is ongoing at MD Anderson. In that trial, patients are randomized to either 6 months of chemotherapy followed by 6 months of observation or 6 months of observation followed by 6 months of chemotherapy. Within this study, a modified peritoneal RECIST measurement in which five locations are measured is being investigated. Because each patient serves as his or her own control, we hope this study will better clarify the true rate of radiographic change for this biologically unique tumor type.

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Disclosures

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