In Reply One of the primary objectives of our recent review\(^1\) on advances in the diagnosis and treatment of metastatic CRC was to emphasize the importance of molecular tumor profiling to customize CRC treatment strategies. Next-generation sequencing panels should be routinely used to identify potentially actionable common mutations, such as KRAS/NRAS/BRAF, as well as rare ones such as NTRK fusions, which are present in less than 1% of CRCs. Drs Bien and Lin highlight NTRK fusions because of the availability of targeted effective therapy and their point underscores the rationale for obtaining multigene panels that evaluate for both common and rare variants, as opposed to specific tests for KRAS/NRAS/BRAF.

We elected not to include discussion of TMB as a biomarker because although it is included in some next-generation sequencing panels, its utility for informing treatment decisions in metastatic CRC remains uncertain. Pembrolizumab was initially approved in a cancer-agnostic fashion for tumors with TMB of 10 mutations per megabase or greater. However, in the KEYNOTE-177 trial, which focused specifically on metastatic CRC, TMB was not a treatment selection criterion.\(^2\) Both the KEYNOTE-158 study and the study by Shrock et al,\(^3\) cited by Bien and Lin, evaluated TMB only among microsatellite instability-high tumors and included too few cases to establish TMB as a predictor of response to immunotherapy in the metastatic CRC population. We agree with Bien and Lin that further investigations of the role of TMB in metastatic CRC would be valuable, but currently there is insufficient evidence to recommend its use in clinical practice.

In addition, we wholeheartedly agree with the comment by Bien and Lin about the critical importance of remediating racial disparities in cancer diagnosis and treatment outcomes. Structural racism pervades US society, health care, and cancer medicine, and its effects are manifest in the disparity between stage-specific survival for Black and White patients with all stages of CRC.\(^4\) For example, a recently published analysis of SEER data\(^5\) assessed the interaction between race/ethnicity and socioeconomic status on the time from CRC to start of treatment. Racial/ethnic groups other than White had longer intervals to treatment initiation; this difference was attenuated by higher socioeconomic status for racial/ethnic groups except among Black patients, among whom higher socioeconomic status was not associated with the interval to treatment start. We agree with Bien and Lin that the reasons for mortality gaps between Black and White patients are multifactorial. Eliminating them requires a multipronged approach pursuing strategies such as increasing the number of Black oncologists, building trust in communities where it is in short supply, ensuring timely access to screening and treatment including clinical trials, and performing next-generation sequencing to ensure that Black patients have equal opportunities to benefit from precision medicine.

Leah H. Biller, MD
Deborah Schrag, MD, MPH

Author Affiliations: Dana-Farber Cancer Institute, Harvard Medical School, Boston, Massachusetts.

Corresponding Author: Deborah Schrag, MD, MPH, 450 Brookline Ave, Boston, MA 02115 (deb_schrag@dfci.harvard.edu).

Conflict of Interest Disclosures: Dr Schrag reports receipt of personal fees from Pfizer (speaking engagement), and research funding from the American Association of Cancer Research and serving as a site primary investigator on a study funded by Grail. No other disclosures were reported.


CORRECTION

Incorrect Positive Predictive Values Reported: In the Review titled “Acute Pancreatitis: A Review,” published in the January 26, 2021, issue of JAMA, incorrect positive predictive values were reported. The sentence under Clinical Presentation and Diagnosis in the Methods section should have read “[C-reactive protein] levels of 190 mg/L or greater within the first 48 hours of admission or an absolute increase of greater than 90 mg/L, have positive predictive values of 31.7% and 27.4% for predicting severe disease, respectively.” This article was corrected online.