Pembrolizumab for Early Triple-Negative Breast Cancer

TO THE EDITOR: In their KEYNOTE-522 trial, Schmid et al. (Feb. 27 issue) found that, among patients with early triple-negative breast cancer, combination therapy with pembrolizumab plus neoadjuvant chemotherapy led to a higher percentage who had a pathological complete response and longer event-free survival than placebo plus neoadjuvant chemotherapy. Identifying histologic and molecular subtypes in patients with triple-negative breast cancer can substantially affect treatment outcome. Burstein et al. identified and confirmed four distinct triple-negative breast cancer subtypes: luminal androgen receptor, mesenchymal, basal-like immunosuppressed, and basal-like immune-activated. Basal-like immunosuppressed tumors were associated with the worst prognoses and basal-like immune-activated tumors were associated with the best prognoses (independent of other known prognostic factors), as compared with the other subtypes. In the current trial, the BRCA mutation profile of the patients was not reported. There is a strong association between BRCA1 mutation and basal-like cancer, and sporadic basal-like breast cancer subtypes show high degrees of chromosomal genomic instability. Telli et al. found that homologous recombination deficiency (HRD) score predicts response to platinum-containing neoadjuvant chemotherapy in patients with triple-negative breast cancer.

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THE AUTHORS REPLY: We agree with the correspondents that it is of interest to assess the BRCA mutation and methylation status in patients with triple-negative breast cancer, given that DNA-repair defects may confer sensitivity to platinum and other agents. Because the KEYNOTE-522 clinical trial did not include a non–platinum-based comparator, analyses of treatment interaction driven by response to platinum-based chemotherapy among biomarker-selected patient populations are not feasible. Indeed, an exploratory end point in our trial involves the examination of molecular biomarkers that might predict clinical response attributable to the addition of pembrolizumab to an appropriate neoadjuvant chemotherapy backbone with anthracycline, taxane, and platinum. These analyses are ongoing.

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Since publication of their article, the authors report no further potential conflict of interest.

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