Comment

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Neoadjuvant Chemotherapy and Immunotherapy in Luminal B–like Breast Cancer: Results of the Phase II GIADA Trial

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Abstract

Purpose: The role of immunotherapy in hormone receptor (HR)-positive, HER2-negative breast cancer is underexplored.

Patients and methods: The neoadjuvant phase II GIADA trial (NCT04659551, EUDRACT 2016-004665-10) enrolled stage II-IIIA premenopausal patients with Luminal B (LumB)-like breast cancer (HR-positive/HER2-negative, Ki67 ≥ 20%, and/or histologic grade 3). Patients received: three 21-day cycles of epirubicin/cyclophosphamide followed by eight 14-day cycles of nivolumab, triptorelin started concomitantly to chemotherapy, and exemestane started concomitantly to nivolumab. Primary endpoint was pathologic complete response (pCR; ypT0/is, ypN0).

Results: A pCR was achieved by 7/43 patients [16.3%; 95% confidence interval (CI), 7.4-34.9]; the rate of residual cancer burden class 0-I was 25.6%. pCR rate was significantly higher for patients with PAM50 Basal breast cancer (4/8, 50%) as compared with other subtypes (LumA 9.1%; LumB 8.3%; *P* = 0.017). Tumor-infiltrating lymphocytes (TIL), immune-related gene-expression signatures, and specific immune cell subpopulations by

multiplex immunofluorescence were significantly associated with pCR. A combined score of Basal subtype and TILs had an AUC of 0.95 (95% CI, 0.89-1.00) for pCR prediction. According to multiplex immunofluorescence, a switch to a more immune-activated tumor microenvironment occurred following exposure to anthracyclines. Most common grade ≥3 treatment-related adverse events (AE) during nivolumab were γ-glutamyltransferase (16.7%), alanine aminotransferase (16.7%), and aspartate aminotransferase (9.5%) increase. Most common immune-related AEs were endocrinopathies (all grades 1-2; including adrenal insufficiency, *n* = 1).

Conclusions: Luminal B-like breast cancers with a Basal molecular subtype and/or a state of immune activation may respond to sequential anthracyclines and anti-PD-1. Our data generate hypotheses that, if validated, could guide immunotherapy development in this context.