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Immune-related adverse events among patients with early-stage triple-negative breast cancer treated with pembrolizumab plus chemotherapy: real-world data from the Neo-Real/ GBECAM-0123 study

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Introduction: Pembrolizumab combined with neoadjuvant chemotherapy is the standard of care for stage II–III triple-negative breast cancer based on the KEYNOTE-522 trial. However, 13% of patients experienced immune-related adverse events (irAEs) of grade ≥3 in the trial. **Objective:** This study aimed to describe patterns of irAEs in a real-world scenario during treatment with pembrolizumab for early-stage triple-negative breast cancer. **Methods:** Patients treated with neoadjuvant pembrolizumab plus chemotherapy across ten Brazilian cancer centers were evaluated in the Neo-Real/ GBECAM-0123 study. The analysis focused on irAE evaluation, including time to onset, management, and association between irAEs and pathological complete response. Logistic regression analyses were conducted to evaluate possible clinical predictors of irAEs. The irAE-free survival was assessed using the Kaplan-Meier method. **Results:** A total of 368 patients were included. Overall, 31.0% of patients (n=114) presented with any grade irAEs. Most of irAEs (72.8%) occurred during the neoadjuvant phase, while 28.1% happened during the adjuvant period. The most frequent irAEs were endocrine (12.8% of the entire cohort), cutaneous (7.6%), and gastrointestinal (7.1%). Fifty patients (13.6%) experienced grade ≥3 irAEs, predominantly gastrointestinal (32.0%). The median duration of irAEs was 29.5 days (range 2–418). Fifty-eight patients (56.0%) needed corticosteroids, and two required additional immunosuppressive therapy. Immunotherapy rechallenge was possible in 54.0% of the cases; permanent discontinuation of pembrolizumab was necessary for 16.0%. No significant association was observed between irAEs and clinic-pathologic features nor pathological complete response status. **Conclusion:** In this real-world analysis, we observed a similar incidence of irAEs as reported in the KEYNOTE-522 trial. Most patients experienced resolution of their irAEs, but some required permanent discontinuation of pembrolizumab. Additionally, there were lasting dysfunctions, particularly endocrine, demanding lifelong support. Careful monitoring and management of these events are essential. Identifying patients who do not require pembrolizumab remains a challenge.

Keywords: triple-negative breast cancer; immunotherapy; drug-related side effects and adverse reactions.