Atezolizumab Plus Nab-paclitaxel in PD-L1–Positive TNBC—Letter

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Narayan and colleagues summarized the results and FDA's review leading to the accelerated approval of atezolizumab in combination with paclitaxel protein-bound for the treatment of patients with unresectable, locally advanced or metastatic triple-negative breast cancer (TNBC), whose tumors express programmed death ligand 1 (PD-L1) based on trial IMpassion130 (1). The authors concluded that despite the immaturity of the overall survival data accelerated approval was appropriate taking into account the potential clinical benefit in terms of progression-free survival in the PD-L1 expressing population. We agree with the authors that atezolizumab plus nab-paclitaxel is an important therapeutic option for patients with PD-L1 immune cell–positive metastatic TNBC. However, it must be underlined that the type of PD-L1 testing used can impact the response to treatment, resulting in potentially different effectiveness across different countries based on the platform and antibody clones adopted. We would like to underline that the barriers to overcome are the lack of standardization of the PD-L1 IHC test methods and test reimbursability.

As no classical clinicopathologic features are associated with PD-L1-positivity, PD-L1 testing is mandatory for patients with advanced TNBC before starting first-line treatment (1, 2). However, it must be underlined that the type of PD-L1 testing used can impact the response to treatment, resulting in potentially different effectiveness across different countries based on the platform and antibody clones adopted. The companion diagnostic test used in the IMpassion130 to select positive patients was Roche Ventana SP142 (Ventana Medical System) PD-L1 IHC assay (2, 3). As reported by Prof. Hope Rugo at ESMO 2019, not all PD-L1 assays are equal, the SP142 portending a stronger predicting value compared to other commercially available anti-PD-L1 antibodies (4). In fact, in previous studies and in our own experience (**Fig. 1**), the clone SP142 displayed greater positivity in inflammatory cells than other anti-PD-L1 antibody clones, such as SP263 by Roche Ventana (Ventana) or 22C3 and 28-8 Dako antibodies (Agilent; ref. 5). In the United States, the FDA approved the VENTANA PD-L1 (SP142) Assay as a companion diagnostic test for selecting patients with TNBC for first-line treatment with atezolizumab, and it is now routinely used. In Europe, the lack of specific guidelines leads to discrepancies in technical and/or clinical validation procedures for PD-L1 testing, which also impacts the efficacy and cost of therapy. In fact, European Medical Agency guidelines suggest to use a validated method to test PD-L1 expression without specifying how to perform a test validation (clinical or technical or both) or indicating the antibody clone or platform to be used.

In conclusion, the effect of PD-L1 testing on the efficacy of atezolizumab depends on the antibody and platform used for patient selection which is related on where the patient lives. The two main barriers to overcome are the lack of standardization of the PD-L1 IHC method and test reimbursability. PD-L1 testing harmonization is an urgency.

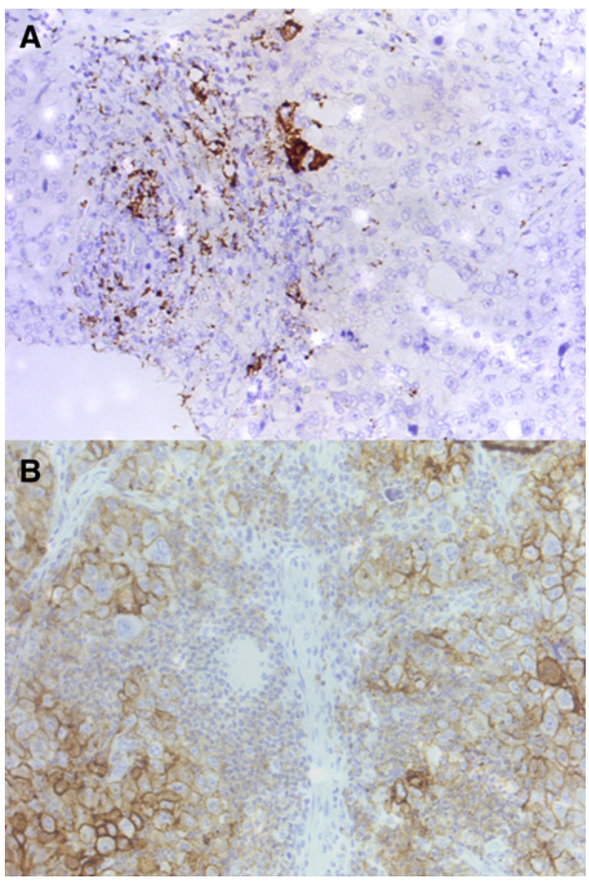

Figure 1.
Paraffin-embedded sections of tissue samples from patients with triple-negative breast cancer stained on the Ventana BenchMark Ultra platform using (**A**) SP142 Roche Ventana antibody: strongly PD-L1–positive lymphocytes and macrophages and negative epithelial cells are present (magnification ×40). **B,** SP263 Roche Ventana antibody: strongly PD-L1–positive epithelial cells and few weakly positive lymphocytes and macrophages are present (magnification ×40).

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Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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