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Response to Jézéquel, Patsouris, Guette, et al.

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We would like to respond to correspondence from Jézéquel et al. (1) regarding our article titled "Immune Checkpoint Profiles in Luminal B Breast Cancer (Alliance)." Currently, the PD-L1–targeting monoclonal antibody atezolizumab is only approved for ER and HER2 disease (1). Our article points out that some high-risk ER-positive breast cancers also have an activated immune microenvironment, and thus exploring immunotherapy in these disease subsets should be actively considered. Jézéquel et al. (2), in their correspondence, suggest a direct cause and effect relationship between immune tolerance and endocrine therapy resistance. We agree there is a correlation, but we remain careful not to project immune tolerance as a direct driver of endocrine therapy resistance. As an alternative, we propose that defects in single-strand DNA damage repair (3–5) are a logical connection between these two biological processes. Jézéquel et al. also suggest that their TNBC C3 cluster is similar to the immune active subset we identified in Luminal B breast cancer. This is certainly an interesting observation, but we remain unsure of the semantics of their argument that "immune response failure" should be equated to "immune tolerance." Immune response failure is a broader term to include immune "cold" tumors. Active immune tolerance is present only when there is a CD8 response that must be opposed for the tumor to exist. Overall, both of us agree that in some ER+ tumors the balance between "immune rejection" and "immune tolerance" could be tipped in favor of rejection with the appropriate immune checkpoint inhibitor.

References

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