TRIPLE-NEGATIVE BREAST CANCER

TRIAL SUMMARY: Early trial of atezolizumab in combination with nab-paclitaxel in patients with mTNBC

Litton JK, Moulder S, Helgason T, et al. Triple-negative first-line study: Neoadjuvant trial of nab-paclitaxel and atezolizumab, a PD-L1 inhibitor, in patients with triple negative breast cancer (TNBC). San Antonio Breast Cancer Symposium, December 6-10, 2016. Abstract OT2-01-14

This paper described the design and recruitment strategy for a phase 1 study of atezolizumab. Atezolizumab is a humanized monoclonal antibody (MAb) that inhibits binding of programmed death ligand 1 (PD-L1) to programmed cell death protein 1 (PD-1) and B7-1, thus restoring tumour-specific T-cell immunity. Combining atezolizumab with chemotherapy is hypothesized to enhance tumour-specific T-cell immunity by exposing the immune system to high levels of tumour antigens and modulating T-cell and natural killer (NK) cell functions. The primary outcome measured in this trial is the pathologic complete response (pCR) in triple-negative breast cancer (TNBC) patients determined to have a chemo-insensitive disease (CID) after anthracycline-based chemotherapy, then treated with atezolizumab + nab-paclitaxel preoperatively.

Treatment-naive patients with localized TNBC underwent a pretreatment biopsy followed by anthracycline-based chemotherapy (AC). During AC, the molecular profile was determined; these results, along with the response assessment (clinical exam/diagnostic imaging), identified CID and guided the second phase of the neoadjuvant chemotherapy.

Patients enrolled in the ARTEMIS (A Randomized, TNBC Enrolling trial to confirm Molecular profiling Improves Survival) trial who were deemed to have CID entered this nonrandomized study. These patients, without response to initial chemotherapy cycles, had a low likelihood (5%) of achieving pCR with additional cycles of chemotherapy. Patients had localized TNBC, as well as adequate organ, bone marrow and cardiac parameters. Exclusion criteria were prior immunotherapy, inflammatory breast cancer, history of autoimmune disease, human immunodeficiency virus (HIV), hepatitis B or C, active tuberculosis and pregnancy.

COMMENTARY: TNBC has an especially poor prognosis in patients whose tumour does not respond to anthracycline and taxane-based chemotherapy. Approximately 50% will have CID, resulting in extensive residual disease at the time of surgery, and 40% to 80% of these patients will recur within 3 years. An anti-PD-L1 approach is attractive for TNBC because this type of cancer is highly mutagenic and produces neoantigens that induce an immune response. TNBC is characterized by an increased number of tumour infiltrating lymphocytes, which can also facilitate immune response. Furthermore, TNBC is associated with high levels of PD-L1 expression compared with other types of breast cancer.

At the 2016 ASCO meeting, the phase 1b trial of atezolizumab in combination with nab-paclitaxel in patients with metastatic TNBC showed promising results. This trial was the first to demonstrate that atezolizumab + nab-paclitaxel is tolerable, with promising activity in mTNBC.

In that context, it will certainly be very interesting to follow results of this early trial, as it could pave the way for a promising new treatment in TNBC.

References

1. Garcia-Teijido et al. Tumor infiltrating lymphocytes in triple negative breast cancer: the future of immune targeting. *Clin Med Insights Oncol* 2016:10(S1) 31-39

IN BRIEF

Already known

- Triple-negative breast cancer (TNBC) is highly mutagenic and produces antigens that induce an immune response.

What this study showed

- A group of patients enrolled in the ARTEMIS trial who showed absence of response to chemotherapy received a combination of atezolizumab and nab-paclitaxel, which was found to be tolerable.

Next steps

- The results presented at San Antonio were from early analyses. If results are confirmed in more patients on longer followup, the combination of atezolizumab and nab-paclitaxel could provide a promising treatment option for patients with TNBC who do not respond to chemotherapy.