Maximizing clinical benefit of atezolizumab in triple negative breast cancer

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In unresectable locally advanced/metastatic triple-negative breast cancer (TNBC), two double-blind placebo-controlled randomized phase III trials evaluating the addition of the immune checkpoint inhibitor (ICI) atezolizumab to single-agent taxane as first-line therapy showed disparate outcomes:
IMpassion130 study demonstrated significantly improved progression-free survival (PFS) and a clinically meaningful effect on overall survival (OS) in patients with PD-L1-positive tumors with the addition of atezolizumab to nab-paclitaxel. However, IMpassion131 showed no significant benefit from the addition of atezolizumab to solvent-based paclitaxel. The key difference including chemo partner difference and steroid criteria prior to receive atezolizumab-base treatment which might deserve to study the potential reason of two RCTs.

For IMpassion130, in the intention-to-treat analysis, the median progression-free survival was 7.2 months with atezolizumab plus nab-paclitaxel, as compared with 5.5 months with placebo plus nab-paclitaxel (hazard ratio for progression or death, 0.80; 95% confidence interval [CI], 0.69 to 0.92; P=0.002); among patients with PD-L1–positive tumors, the median progression-free survival was 7.5 months and 5.0 months, respectively (hazard ratio, 0.62; 95% CI, 0.49 to 0.78; P<0.001). In the intention-to-treat analysis, the median overall survival was 21.3 months with atezolizumab plus nab-paclitaxel and 17.6 months with placebo plus nab-paclitaxel (hazard ratio for death, 0.84; 95% CI, 0.69 to 1.02; P=0.08); among patients with PD-L1–positive tumors, the median overall survival was 25.0 months and 15.5 months, respectively (hazard ratio, 0.62; 95% CI, 0.45 to 0.86). Atezolizumab plus nab-paclitaxel prolonged progression-free survival among patients with metastatic triple-negative breast cancer in both the intention-to-treat population and the PD-L1–positive subgroup.

For IMpassion131, at the primary PFS analysis, adding atezolizumab to paclitaxel did not improve investigator-assessed PFS in the PD-L1-positive population [hazard ratio (HR) 0.82, 95% confidence interval (CI) 0.60-1.12; P = 0.20; median PFS 6.0 months with atezolizumab-paclitaxel versus 5.7 months with placebo-paclitaxel]. In the PD-L1-positive population, atezolizumab-paclitaxel was associated with more favourable unconfirmed best overall response rate (63% versus 55% with placebo-paclitaxel) and median duration of response (7.2 versus 5.5 months, respectively). Final OS results showed no difference between arms (HR 1.11, 95% CI 0.76-1.64; median 22.1 months with atezolizumab-paclitaxel versus 28.3 months with placebo-paclitaxel in the PD-L1-positive population). Results in the ITT population were consistent with the PD-L1-positive population. The safety profile was consistent with known effects of each study drug.