TPS632 Poster Session

# OPERETTA: A phase II study evaluating neoadjuvant and adjuvant olaparib plus pembrolizumab following platinum-based chemotherapy plus pembrolizumab for germline BRCA mutated triple negative breast cancer.

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**Background:** Triple negative breast cancer (TNBC) remains the most challenging phenotype of breast cancer. There is still an unmet clinical need for improving the fine-tuning of indications for targeted treatments in this population. In TNBC, the frequency of germline BRCA (gBRCA) 1/2 mutations was reported to be up to 19.5%. This has led to promising clinical strategies based on poly adenosine diphosphate (ADP)-ribose polymerase inhibitors that inhibit single-stranded DNA damage repair and/or modified chemotherapy approaches targeting the DNA damage response, using platinum-based regimens. Based on the results of the OlympiA and KEYNOTE522 study, the adjuvant treatment with olaparib for gBRCAm and neoadjuvant and adjuvant pembrolizumab for patients with a high risk of recurrence TNBC has been treatment options as the standard of care. We hypothesize that neoadjuvant and adjuvant combination treatment with olaparib and pembrolizumab following combination treatment with platinum-based chemotherapy and pembrolizumab would synergistically increase the anti-tumor effect through the enhancement of immunogenicity and DNA damage in patients with gBRCA mutated breast cancer. **Methods:** OPERETTA is a multi-centered, prospective single-arm phase II feasibility study of patients treated with neoadjuvant olaparib plus pembrolizumab following platinum-based chemotherapy plus pembrolizumab in gBRCA 1/2 mutated TNBC. The patients with stage IIA-IIIB TNBC known as gBRCA 1/2 mutated will be registered. The primary objective is the pCR rate defined as the absence of residual invasive disease in the breast and axilla. The secondary objectives include additional efficacy measures (i.e., Residual Cancer Burden [RCB] 0/1rate, 3 years overall survival [3y-OS], 3 years event-free survivals [3y-EFS]), and safety. The estimated sample size using Simon's two-stage design, with a null hypothesis of a 45% pCR rate and an alternative hypothesis of 70%, was calculated. Given a significance level of 0.1 and 80% power, the design allows a maximum of 23 patients to be included. Eligible patients will be received combination treatment with paclitaxel (80 mg/m2 qw), carboplatin (AUC 1.5 qw or AUC 5 q3w), and pembrolizumab (200mg q3w) for first 12 weeks followed by olaparib (300mg BID) with pembrolizumab (200mg q3w) for another 12 weeks as neoadjuvant treatment. Breast/axillary surgery and radiotherapy are recommended per standard of care. After surgery, the combination of olaparib plus pembrolizumab will be continued for another 27 weeks as adjuvant treatment. This study is recruiting in Japan, and 2 patients are enrolled as of January 2025. This study is part of the West Japan Oncology Group (WJOG) breast cancer study group: WJOG14020B. Clinical trial information: NCT05485766. Research Sponsor: Merck; AMED.