Tumor Board Tuesday – Dr. Jane L. Meisel & Dr. Dionisia Quiroga, 12/20/2022:
BRCA mutated 2L Tx

Posttest Rationale

1. **What second-line therapy would you select for a patient with PD-L1-negative, HR-, HER2- (IHC 0) metastatic BC who received first-lien treatment with carboplatin/gemcitabine and whose disease was found to be *BRCA+* after recurrence during cycle 6 of treatment with liposomal doxorubicin?**
    a. Olaparib
    b. Paclitaxel
    c. Pembrolizumab + chemo
    d. Sacituzumab govitecan

Rationale: Both olaparib and talazoparib are NCCN guideline preferred treatment options for BRCA1/2+ breast cancer of any subtype, though they are FDA-indicated for HER2- BC. Olaparib is likely the best choice because it has demonstrated a significantly longer mPFS (7.0 vs 4.2 months), a higher ORR (59.9% vs 28.8%), and a lower incidence of grade ≥3 adverse events (36.6% vs 50.5%) compared with physician's choice chemotherapy in patients who had received ≥2 previous chemotherapy regimens for metastatic disease. Treatment with talazoparib vs physician's choice chemotherapy in patients who had received ≤3 previous cytotoxic regimens demonstrated a significantly longer mPFS (8.6 vs 5.6 months), a higher ORR (62.6% vs 27.2%), and a similar incidence of grade 3/4 adverse events (25.5% vs 25.4%). Pembrolizumab + chemotherapy is a preferred first-line therapy for TNBC. Sacituzumab govitecan is a preferred option for patients with TNBC who have received ≥2 prior therapies, with at least 1 line for metastatic disease.

References: Robson ME, Tung N, Conte P, et al. OlympiAD final overall survival and tolerability results: Olaparib versus chemotherapy treatment of physician's choice in patients with a germline BRCA mutation and HER2-negative metastatic breast cancer. *Ann Oncol*. 2019;30(4):558-566. doi:10.1093/annonc/mdz012

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2. **All patients with metastatic BC and which of the following should be tested for *BRCA* mutations?**
    a. HER2- at diagnosis
    b. HER2- after 3 lines
    c. TNBC at diagnosis
    d. TNBC after 3 lines

Rationale: Any patient with newly-diagnosed, HER2- breast cancer who meets the eligibility criteria for a PARP inhibitor treatment should be offered germline testing. Additionally, the NCCN panel supports the use of PARP inhibitor therapy in any breast cancer subtype associated with a germlien *BRCA1/2* mutation (FDA indicated for HER2- BC only) and recommends assessment for germline *BRCA1/2* mutations in all patients with recurrent or metastatic breast cancer.

Reference: Tung N, Garber JE. PARP inhibition in breast cancer: progress made and future hopes. *NPJ Breast Cancer*. 2022;8(1):47. doi:10.1038/s41523-022-00411-3

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