Tumor Board Tuesday – Dr. Paolo Tarantino & Dr. Caterina Sposetti, 7/19/22:

1st Line Treatment and Management of *BRCA* Mutated Metastatic Breast Cancer

Posttest Rationale

1. **Which first-line therapy would you select for a patient with PD-L1 negative (CPS≤10), *BRCA1/2*+ mTNBC relapsed after prior adjuvant chemotherapy (DFI 30 months)?**

    a. Taxane-Pembrolizumab
    b. Single-agent ChT
    c. PARPi
    d. Combination ChT

Rationale: Considering PD-L1 CPS ≤10, Taxane-Pembrolizumab is not indicated. Combination ChT is recommended only for patients with rapid progression of disease, visceral crisis and/or need for rapid symptoms/disease control. OlympiAD and EMBRACA phase III trials showed significant benefit in PFS of 2.8 months and 3.0 months for Olaparib (HR 0.58; 95% CI 0.43, 0.80; *P* < .001) and Talazoparib (HR 0.54; 95% CI 0.41, 0.71; *P* < .001), respectively, compared to physician's choice chemotherapy. Indeed, the preferred treatment option in this case is a PARPi. However, in final results, neither Olaparib nor Talazoparib group showed significant OS improvement compared to physician's choice chemotherapy group.

In light of the almost equal efficacy showed by these two PARPi, treatment choice usually relies on their toxicity profile, with Olaparib being associated with slightly more GI toxicity, while Talazoparib being associated with slightly higher incidence of hematological AEs. Safety of both drugs is overall good, with mainly G1/G2 AEs, and PROs and QoL studies highlighted significant improvements in global health status with PARPi compared to ChT.

For a patient with a previous history of severe hematological toxicity during ChT, Olaparib is the preferred option.

References: National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®): Breast Cancer (v2.2022). Updated December 20, 2021. Accessed April 13, 2022. https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf

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