Tumor Board Tuesday – Dr. Elenora Teplinsky, 02/07/2023:
HER2+ Low Equivocal Breast Cancer

Posttest Rationale

1. **What treatment would you select for a 60-year-old woman with ER+/PR-/HER2-low mBC who most recently experienced disease progression in the liver and pleura after 5 months on paclitaxel (previously treated with AI + CDK4/6 inhibitor, fulvestrant, everolimus + exemestane, and capecitabine)?**

    a. Back to endocrine therapy
    b. Eribulin
    c. Gemcitabine
    d. Trastuzumab deruxtecan

Rationale: Given the patients prior treatments and that she has HER2-low mBC, trastuzumab deruxtecan is likely the best treatment option at this time. Trastuzumab deruxtecan recently received FDA approval as indicated for the treatment of patients with unresectable or metastatic HER2-low (IHC1+ or IHC2+/ISH-) breast cancer who have received prior chemotherapy in the metastatic setting or experienced disease recurrence during or within 6 months of adjuvant chemotherapy. This approval is based on results form the phase 3 DESTINY-Breast04 trial: among all patients, treatment with trastuzumab deruxtecan compared with physician's choice significantly improved mPFS (9.9 vs 5.1 months; HR 0.50) and mOS (23.4 vs 16.8 months; HR 0.64), along with a greater ORR (52.3% vs 16.3%).

Reference: ENHERTU® (fam-trastuzumab deruxtecan-nxki) [prescribing information]. Daiichi Sankyo, Inc. Approved 2019. Revised November 2022. https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=761139

Modi S, Jacot W, Yamashita T, et al. Trastuzumab Deruxtecan in Previously Treated HER2-Low Advanced Breast Cancer. N Engl J Med. 2022;387(1):9-20. doi:10.1056/NEJMoa2203690

2. **What subsequent treatment would you select for this 60-year-old woman with ER+/PR-/HER2-low mBC if she experienced disease progression while receiving trastuzumab deruxtecan?**

    a. Doxorubicin
    b. Eribulin
    c. Gemcitabine
    d. Sacituzumab govitecan

Rationale: Sacituzumab govitecan is likely the best choice for this patient; it has recently received FDA approval as indicated for the treatment of patients with unresectable locally advanced or metastatic ER+/HER2-low (IHC0, IHC1+, or IHC2+/ISH-) breast cancer who have received endocrine therapy and at least 2 additional systemic therapies in the metastatic setting. This approval is based on the results from the phase 3 TROPiCS-02 trial, wherein treatment with sacituzumab govitecan compared with physician's choice significantly improved mOS (14.4 vs 11.2 months; HR 0.79), ORR (21% vs 14%; OR 1.63), and quality of life.

Reference: TRODELVY® (sacituzumab govitecan-hziy) [prescribing information]. Immunomedics, Inc. Approved 2020. Revised February 2023. https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=761115

Rugo HS, Bardia A, Marmé F, et al. LBA76 Overall survival (OS) results from the phase III TROPiCS-02 study of sacituzumab govitecan (SG) vs treatment of physician's choice (TPC) in patients (pts) with HR+/HER2- metastatic breast cancer (mBC). Ann Oncol. 2022;33:S1386. doi:10.1016/j.annonc.2022.08.012