

**SAFETY AND EFFICACY OF GEMCITABINE AND TRASTUZUMAB COMBINATION IN HEAVILY PRETREATED PATIENTS WITH HER2-POSITIVE METASTATIC BREAST CANCER**

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**Introduction - Purpose :** Prognosis of HER2-positive metastatic breast cancer (MBC) has been dramatically improved by trastuzumab (Tmab). More recently, newer anti-HER2 agents such as lapatinib, pertuzumab and T-DM1 have prolonged survival. Despite the efficacy of these drugs, most patients develop progressive disease during or after treatment, and alternative anti-HER2 agents plus chemotherapies are required in subsequent lines of treatment. However, there are few evidence on efficacy of Tmab-containing regimens after disease progression. Gemcitabine (GEM) is non-cross resistant to anthracycline and taxane. Preclinical studies have shown that the combination of Tmab and GEM has synergistic effect against HER2-positive breast cancer cell lines. In this study we assessed the efficacy and safety of the combination of Tmab and GEM in patients with HER2-positive MBC previously treated with anti-HER2 therapy.

**Methods - Tools :** In this study we evaluated patients treated with one or more anti-HER2 directed regimens for MBC in the Medical Oncology Department of Bülent Ecevit University. Patients were administered with GEM 1250 mg/m<sup>2</sup> on days 1 and 8 of each 21-day cycle and Tmab 4mg/kg loading dose and then 2mg/kg weekly. The primary endpoint was objective response rate (ORR). Secondary endpoints included progression free survival (PFS), overall survival, and safety.

**Findings :** 30 patients were enrolled. Patients had ER positive tumor (33.3%), a median of 2 metastatic organ sites, visceral metastasis (76.7%), prior (neo) adjuvant Tmab (30.0%) and a median of 2 prior chemotherapy regimens for MBC. Previous HER2-directed drugs included Tmab (100%), and lapatinib (66.7%), ORR was 23.3% (95% CI, 8.6%-36.8%). Median PFS was 186 days. Patients with response received a median of 8 cycles (6-18 cycles) of treatment. Grade3/4 leukopenia (23.0%) and neutropenia (38.6%) were observed. All non-hematological toxicities were less than grade 3.

**Discussion :** The Combination Tmab and GEM is effective and well-tolerated regimen for patients previously treated with HER2-directed therapy, and appears to make disease stable for long time period.

**Keywords:** HER2-positive, breast cancer, metastatic, gemcitabine, trastuzumab