Survival of Hormone Receptor-Positive, HER2-negative Metastatic Breast Cancer that had Progressed on Previous Nonsteroidal Aromatase Inhibitors with or without Everolimus and Exemestane Combination

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**Background:** Everolimus combined with exemestane has been shown to improve progression free survival (PFS) in patients with endocrine-resistant metastatic breast cancer (MBC). The regimen has been well-accepted despite lack of survival benefit. In real-life setting, patients were not well-selected and hence benefit of such treatment may not be as robust.

**Methods:** This is a retrospective review of 143 hormone receptor (HR) positive, human epidermal growth factor receptor type 2 (HER-2) negative MBC patients in Ramathibodi cancer registry progressing on nonsteroidal aromatase inhibitors (NSAI). Pts who received everolimus/exemestane combination in any lines of therapy (EE group) were compared to no everolimus (NE group). The primary end point was overall survival (OS) adjusted to prognostic factors. Secondary end points were subgroup analysis of OS and progression-free survival of the cohort.

**Results:** There were 52 pts in EE group and 91 pts in NE group. Mean age was 58.6 years. Majority had Eastern Cooperative Oncology Group score 0-1 and < 2 metastatic organ-sites (76%). Visceral involvement in EE and NE were 79% and 67%, respectively (p = 0.13). Sixty-six and 58% of EE and NE, respectively, were treated with first line NSAI (p = 0.56). Three-quarters of patients received everolimus 10 mg daily with 44% required dose reduction. Median follow-up time was 51 months. Unadjusted median OS was significantly longer in EE [33 vs. 25 months, hazard ratio (HR), 0.66 (95%CI 0.44-0.998); p = 0.049]. In univariate analysis, factors affecting survival included numbers of metastatic sites, presence of bone metastasis, treatment with EE, and numbers of line of treatment after NSAI failure. Factors that remained significant upon multivariate analysis were numbers of line of treatment [HR 0.71 (95%CI 0.63-0.79); p < 0.05] and numbers of metastatic site [HR per one site increase 1.35 (95%CI 1.05-1.73); p = 0.02]. Median numbers of treatment line after NSAI failure was 5.2 vs 3.6 lines in EE and NE, respectively. Median OS in those treated with EE in first (N=14), second (N=18) and third (N=20) line after NSAI-failure were 23, 21 and 38 months, respectively, compared to 25 months with NE [HR 0.91, 0.74, 0.499; (p = 0.16, log rank)]. PFS in pts receiving EE as first Rx after NSAI was numerically longer compared to those who received other agents (capecitabine, taxanes, fulvestrant, exemestane) after NSAI [10 vs. 4-7 months, p >0.05].

**Conclusions:** In this real-life practice data, pts with hormone receptor positive, HER-2 negative MBC who had progressed on NSAI, the sequential use of multiple treatment regimens of endocrine and chemotherapy is an essence to longer survival. Everolimus/ exemestane may have contributed, to a lesser extent, to improvement in survival. Efficacy of EE appeared to be maintained when used in later line of treatment in these heavily pretreated patients.