**Combination of endocrine therapy, gonadotropin-releasing hormone agonist, and immunotherapy enhance immune activation in premenopausal ER+/HER2- metastatic breast cancer patients: final updates from PEER study**

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**Purpose:**

In metastatic breast cancer (MBC), immunotherapy is effective in triple-negative, but not in ER+/HER2-patients. Here we report the final updates of the survival and biomarker analysis from ER+/HER2- MBC patients in PEER study.

**Material & methods:**

Premenopausal ER+/HER2- MBC patients failed ≤2 lines of ET without chemotherapy for MBC were enrolled in National Taiwan University Hospital (NCT02990845). Patients received exemestane, leuprolide, and pembrolizumab. The primary endpoint was progression-free survival (PFS) rate at 8 months. The secondary endpoints included overall response rate (ORR), overall survival (OS), PFS, and other biomarkers (including tumor-infiltrating lymphocyte (TIL), PD-L1 expression, RNAseq, and IO360 analysis).

**Results:**

Between 2017 and 2020, 14 of 15 enrolled patients were evaluable. PFS rate at 8 months was 64.3% and the ORR was 35.7%. At a median follow-up of 41.5 months, the median PFS and OS were 10.3 and 39. 6 months. The median OS in partial response, stable disease, and progressive disease patients were 39.6, 51.8, and 17.6 months respectively. In both RNAseq and IO-360 analyses, no difference in immune cell abundance was noted among responder versus non-responder patients from pre-treatment tumor samples. In the IO-360 analysis, upregulation of genes in the immune cell related signature and increased CD45+ cells were noted from post-treatment tumor samples. In RNAseq analysis, upregulation of immunoglobulin related signature was noted from pre-treatment tumor samples in responders. Most immune cell populations are increased after treatment.

**Conclusion:**

Adding ET and GnRHa to immunotherapy is effective for premenopausal ER+/HER2- MBC, with activation of immune system.