

**[P5-13-03] Fulvestrant plus anastrozole as neoadjuvant therapy in postmenopausal women with hormone receptor positive early breast cancer**

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**Background:** Aromatase inhibitors (AIs) are effective in reducing the risk of recurrence from breast cancer (BC) but 20% of patients (pts) with early BC still recur despite adjuvant AIs. Thus more effective endocrine therapies (HTs) are needed. In metastatic BC (MBC), combination of lower dose fulvestrant plus anastrozole improves survival compared to anastrozole alone. The 21-gene Recurrence Score® (RS; Oncotype DX®) has been validated to predict benefit from adding chemotherapy (CT) to HT where pts with a low score have little benefit from CT and derive a large benefit from HT. Ki-67 response to neo-adjuvant HT may predict adjuvant outcomes to HT. Postoperative Endocrine Prognostic Index (PEPI) and modified PEPI may further identify a subset of HT sensitive cancers that do not require adjuvant CT (PEPI 0 category). We conducted a single arm phase II trial to assess the efficacy of fulvestrant plus anastrozole as neoadjuvant HT in pts with operable BC.

**Methods:** Postmenopausal pts with stage II and III, ER/PR+, HER2 (-) BC with a RS<25 (performed on initial core bx) were included. Duration of neo-adjuvant HT was 4 months. Pts received anastrozole 1mg (PO) daily continuously from day 1 until surgery + fulvestrant (IM) 500mg on day 1, 14 and 28 of cycle 1, and on the last day of three subsequent 28 day cycles (total 6 doses of fulvestrant). At week 4, an optional core bx was repeated to assess change in Ki-67.

Response assessments were made clinically every 4 wks. All pts had breast/axillary surgery after the 6<sup>th</sup> dose of fulvestrant. Ki-67, histologic grade, ER/PR status, and RS were assessed at baseline, core bx at 4 wks, and at definitive surgery. Primary end points were pathologic complete response (pCR) rate and change in Ki-67. Adjuvant CT was left to the discretion of treating physician.

**Results:** 42 pts were enrolled 7/2009 to 11/2014. Median age was 62. 32 (76%) patients had stage IIA, 7 (17%) had stage IIB and 3 (7%) had stage III disease. 14% had clinically node positive disease. The median RS was 12 (0-24). Median tumor size was 3.5cm. 21%, 74%, and 5% had grade 1, 2 and 3 tumors respectively. Mean ER expression was 95%. 16 (38%) pts had a clinical complete response (cCR), 13 (31%) had a clinical partial response (cPR) and 12 (29%) had stable disease. One pt had progression on therapy. There were no pCRs. Median baseline Ki-67 was 5% (1-36%). 94% of pts had decrease in Ki-67 from baseline to 4-week bx and 97% of pts had decrease in Ki-67 from baseline to surgery. Modified PEPI score at surgery was 0 in 53% of patients. 78% of pts did not receive adjuvant CT. At median follow up of 38 mos only 1 pt had a recurrence with 98% free of a recurrence. There were no grade 3 or grade 4 toxicities.

**Conclusions:** The neoadjuvant combination of anastrozole and fulvestrant in pts with RS<25 markedly improves Ki-67 response with more than half of pts achieving a modified PEPI score of 0 at surgery. At a relatively short median follow up, recurrence rate is very low. Given the efficacy and tolerability of anastrozole plus fulvestrant in MBC and now in the neo-adjuvant setting, an adjuvant trial of this combination is warranted in pts with ER+ BC.

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**Poster Session 5: Treatment: Neoadjuvant Endocrine Therapy (5:00 PM-7:00 PM)**

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