Oncotype DX and proliferation response to short-term preoperative endocrine therapy for chemotherapy decision in early breast cancer: Biomarker data from the prospective multicenter phase II/III WSG-ADAPT trial.

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Background: WSG-ADAPT aims to optimize early breast cancer therapy within a genomically classified (by OncotypeDX) intermediate-risk group using individual endocrine sensitivity. Methods: WSG-ADAPT HR+/HER2- analyzes biomarker changes after 3 weeks of preoperative ET [aromatase inhibitors (AI) in postmenopausal, tamoxifen (Tam) in premenopausal women]. Overall, n=1760 patients (HR+/HER2-, pN0-1) with Recurrence Score (RS) 0-11 or RS 12-25 and post-Tx Ki-67<10% are treated by ET alone. Other RS 12-25 and all RS ≥26 patients are included in phase III CTx design (n=2200). Results: 1118 patients from 61 centers have been enrolled (01/2014); run-in phase analysis included 383 patients (median age 54 years, 175 Tam, 208 AI). RS distribution (≤11/12-25/≥26) was 23%/57%/20%; median relative Ki-67 decreases were 0.67/0.60/0.40 by RS groups (p=0.017). Median relative Ki-67 decrease was more pronounced in post- vs. premenopausal patients (75% vs. 38%; p<0.001). Mean PR (not ER) expression changes were also more pronounced in postmenopausal patients (-39.5 %- vs. -10.4%-units; p<0.001). Pre- and post-endocrine RS (n=187) are moderately correlated (rs = .70, p<.001); no significant RS change was seen (95% CI: -1.7 to 0.3). Absolute change in Ki-67 by IHC was correlated with change in RS proliferation (rs = .62, 95% CI: 0.52 to 0.7). Median ER expression by RT-PCR was higher in post- than premenopausal patients (10.25 vs. 9.3, p<0.001); median PR expression by RT-PCR trended oppositely (7.7 vs. 8.1, p=0.01). Baseline ER expression by RT-PCR (not IHC) was associated with relative Ki-67 decrease (rs = .29, p<0.001). Baseline Ki-67, menopausal status/endocrine agent, and RS were independent predictors for post-treatment Ki-67. Conclusions: Postmenopausal patients (mostly AI) and those with lower baseline RS showed stronger proliferation response to short preoperative endocrine therapy. The difference in outcome between early proliferation responders (>70%) treated with ET alone among pN0/N1 patients with RS 12-25 and those with RS<11 will be tested in the WSG-ADAPT HR+/HER2- main phase. Clinical trial information: NCT01779206.