[P6-05-11] Run-in phase of prospective WSG-ADAPT HR+/HER2- trial demonstrates feasibility of early endocrine sensitivity prediction by recurrence score and conventional parameters in clinical routine

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Background: Despite promising evidence regarding outcome prediction, endocrine sensitivity, as determined by proliferation response to short-term preoperative endocrine therapy, is currently not included in adjuvant chemotherapy decisions in early HR+/HER2- breast cancer (BC).
Methods: The prospective WSG-ADAPT HR+/HER2- trial includes early BC patients with 0-3 positive LN who are candidates for adjuvant chemotherapy based on clinical-pathological criteria alone; it aims to spare chemotherapy in a substantial proportion utilizing a combination of genomic assessment by Oncotype DX and endocrine sensitivity testing. All patients received 3-week preoperative endocrine induction therapy (ET): aromatase inhibitors (AI) if postmenopausal, tamoxifen if premenopausal. Patients with low (0-11) Recurrence Score (RS) or intermediate RS (12-25) and ET response (centrally tested, post-therapy Ki-67 <10%) are recommended to forego adjuvant chemotherapy ("low-risk" patients). Distribution of RS, responder percentages in each group, and impacts of RS, ET regimen, and initial Ki-67 on post-therapy Ki-67 are reported here.
Results: As of 6/2013, 380 patients from 30 study centers had been enrolled in the ADAPT HR+/HER2- trial. Median age was 54 years. At first pre-planned analysis (5/2013), paired Ki-67 measurements (pre-/post-therapy) were available in 241 patients; RS was available in 208 cases (201 with paired Ki-67). RS was low in 21.6%, intermediate in 57.7%, and high in 20.7%; the respective risk group responder percentages (post-treatment Ki 67 <10%) were 84.1%, 73.9%, and 40.0% ($p<0.001$ when comparing low/intermediate vs. high, chi-square). In particular, these percentages support the pre-trial estimate of >70% endocrine responders in the intermediate genomic risk group, who could potentially be spared adjuvant chemotherapy. Median Ki 67 level decreases (as percentage of pre-treatment value) were 25% in premenopausal patients (tamoxifen, n=101) vs. 75% in postmenopausal patients (AI, n=115) ($p<0.001$, Mann-Whitney); median decreases by RS group were similar, 61% (low), 53% (intermediate) and 56% (high), respectively ($p=0.81$, Kruskal-Wallis). In linear regression, pre-treatment Ki-67, endocrine regimen/menopausal status, and RS were all independent predictors for post-treatment Ki 67. Final run-in-phase analysis and validation will be presented after completion of endocrine induction therapy in 400 patients.
Conclusions: The Run-In Phase of the WSG ADAPT HR+/HER2- trial confirms trial design estimates of RS and proliferation response to induction ET. It indicates that the multicenter prospective ADAPT concept combining static and dynamic biomarker assessment for individualized therapy decisions in early BC is feasible. Proliferation response was strongly associated with therapy group (AI/post-menopausal vs. tamoxifen/pre-menopausal). Survival non-inferiority of intermediate Recurrence Score proliferation responders vs. low Recurrence Score patients (active control) will be tested in the ADAPT main phase to determine if adjuvant chemotherapy can be spared in 70% of patients with 0-3 positive LN classified as "intermediate risk" by conventional factors.

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Poster Session 6: Tumor Cell and Molecular Biology: Biomarkers (7:30 AM-9:00 AM)