P231 Luminal subtypes vs. early Ki-67 response and Oncotype DX® in early breast cancer: WSG-ADAPT study

Poster Abstracts II

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Goals: WSG-ADAPT aims to optimize early breast cancer (eBC) therapy within distinct subtypes of BC based on individual early proliferation response. Endocrine sensitivity combined with OncotypeDX® is used to guide chemotherapy decision within the HR+/HER2? subtype.

Methods: WSG-ADAPT (target n?=?4950) analyzes biomarker changes after 3 weeks of subtype-specific therapy. For the HR+/HER2? subtype, preoperative ET is given for 3 weeks prior to surgery/biopsy [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 Ki67 <10% are treated by ET alone. Other RS 12–25 and all RS ?26 patients are included in phase III CTx design (n?=?2200). Aim of the present analysis is a first prospective comparison of local and central pathology to OncotypeDX® on core biopsies. Measures of concordance included gamma statistic and Spearman (rank) correlations.

Results: Within ADAPT HR+/HER2?, 2058 patients from 79 centers have been enrolled as of 11/2014. For quality assurance, a correlative analysis in the first n?=?800 patients with complete baseline documentation was performed. For histological grade, concordance was only 63.5% on diagnostic core biopsies (??=?0.70). Remarkably, 72% of centrally G3 tumors were assessed as G1–G2 by the local lab. Central grade was more strongly associated with RS than local grade (rank correlation 0.40 vs. 0.24). For Ki67, the rank correlation of local with central measurements was 0.64; central Ki67 had a slightly higher correlation with RS than local Ki67 (0.48 vs. 0.41). Defining “luminal B-type” as Ki67 >20% and/or PR <20%, local IHC has 26% discordance with central luminal B vs. A; including G3 in the definition, discordance is also 26%. The ADAPT design (no adjuvant chemotherapy if RS 12–25/postendocrine Ki67 <10% or RS 0–11) would spare 46% of chemotherapy indications based on locally assessed luminal B with or without the G3 criterion.

Conclusion: The present analysis confirms our prior observations regarding discordance of prognostic tools in HR+/HER2? eBC. Further quality control in pathology is a prerequisite for conclusive statements on the role of single markers (grade, Ki67, PR, and genomic signatures) in intermediate-risk eBC. Combining RS with individual early response to endocrine therapy could

spare adjuvant chemotherapy in a substantial subset of luminal B eBC.