Hormone receptor discordance between local and central pathology with RT-PCR analysis: Results from multicenter Phase III WSG-PlanB trial.

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Background: Discordances between local and central pathology regarding ER, PR, and HER2 status may occur at varying frequencies, which may be attributable to technical factors (tissue handling, inter-observer variability) or to underlying disease heterogeneity. Our aim was to analyze local and central ER/PR status among samples acquired in a randomized clinical trial for associations with clinical and pathological parameters.

Methods: PlanB accrued 3,198 patients with primary HER2- breast cancer to (i) optimize prognostication using Recurrence Score (RS) and (ii) compare adjuvant anthracycline-free (docetaxel/cyclophosphamide) to anthracycline-containing chemotherapy (EC-Doc). Recently, WSG-Plan B provided first prospective phase III survival data for Oncotype DX with 98% 3y EFS for low and intermediate risk RS. Patients were entered based on local immunohistochemistry (IHC) but also centrally tested (ER/PR, grade, Ki67). Here, discordant cases were identified, rechecked, and analyzed regarding clinical/pathological parameters including quantitative ER/PR (Oncotype DX).

Results: RS and both local and central ER / PR were available in n = 2170 patients; 58 (median age 50.5y) had discordant local vs. central ER and/or PR status. Receptor discordant cases more often presented with > 3 lymph nodes (15.5% vs. 5.4%, p = 0.001), local G3 (53.4% vs. 21.8%, p < 0.001), central G3 (50.0% vs. 31.4%, 0.013), high Ki67 (81.8% vs. 50.5%, p < 0.001) and RS > 11 (94.7% vs. 81.6%, p = 0.004). Discordant cases were less frequently positive for quantitative ER (52.6% vs. 98.9%, p < 0.001) and PR (42.1% vs. 86.2%, p < 0.001) and had lower mean % central ER (7.5% vs. 91.8%, p < 0.001) and PR (21.0% vs. 62.7%, p < 0.001). Concordance between quantitative HR (Oncotype DX) and central IHC was higher than with local HR.
Conclusions: Overall, excellent concordance (97.3%) was found for ER and PR between local and central pathology. Cases with discordant HR status between local and central pathology present with more aggressive biology and lower quantitative HR measurements compared to concordant HR positive disease. The clinical consequences will become apparent as follow up matures in this study. Clinical trial information: NCT01049425