Prospective comparison of Recurrence Score, uPA/PAI-1, central grade and molecular classification in early breast cancer: Interim results from the WSG-Plan B trial.

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Abstract Disclosures

Abstract:

**Background:** Both the recurrence score (RS) multi-gene assay and invasion factors uPA/PAI-1 are included in guidelines (ASCO, AGO) for decision support regarding adjuvant chemotherapy in early breast cancer (BC). Here we present the first preplanned WSG-Plan B trial correlation analysis of RS, uPA/PAI-1, and molecular subtypes by protein expression.

**Methods:** Plan B trial (n=2,448) is evaluating anthracycline-free adjuvant chemotherapy (6x TC) vs. 4xEC-4xDOC in HER2-negative BC. RS is used as selection criterion for chemotherapy or hormonal therapy alone; uPA/PAI-1 (by ELISA) is obtained as an optional risk factor. Central and Ki-67-modified grade and luminal B subtype (by 13.25% or 20% Ki-67 cut-offs) evaluation are performed by the independent trial pathologist.

**Results:** From April 2009 to February 2011, 2380 patients have been recruited and 1806 randomized to the study. In 1106 pts, both RS and central grade, in 592, both Ki-67 and RS, and in 201 uPA/PAI-1 and RS were available. When considered as continuous variables, RS was weakly positively correlated (Spearman’s coefficient
rs) with PAI-1 (rs=0.21, p=0.003), Ki-67 (rs=0.336, p<0.001), and central grade (rs=0.498, p<0.001). When considered as risk categories, there was only a weak concordance between RS and uPA/PAI-1, using either standard RS (18; 30) or PlanB cut-offs (low risk <11 RS), with 67% of patients having high uPA/PAI-1 within the low/intermediate-RS subgroups. 29-33% of G3 tumors are allocated to the RS low-risk group. While RS high-risk was predictive of high risk by uPA/PAI-1, grade and luminal B subtype, the converse was not true; clinically relevant proportions (between 33-66%) of patients identified by uPA/PAI-1 and Ki-67 as being at high risk have low/intermediate RS. Conclusions: For the first time, risk groups according to RS, Ki-67 and uPA/PAI-1 have been prospectively compared. These preliminary data show that the high RS group seems predictive of high uPA/PAI-1, aggressive central grade and luminal B subtype, but the converse is not true; these markers do not predict the RS. Further evaluation within the Plan B trial will clarify the clinical significance of these findings.