biomarkers in breast cancer (prognostic, predictive and pharmacodynamic)

AP-2gamma as a novel biomarker of endocrine resistance: Results from the TransCONFIRM study

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Background: AP-2gamma is a transcription factor implicated in the biology of breast cancer (BC). However, the prognostic role of AP-2gamma in BC is controversial and little is known about its predictive value for endocrine therapy. We recently conducted a gene expression study on BC samples from patients (pts) enrolled in the CONFIRM trial, which compared Fulvestrant (Ful) 500 mg vs 250 mg in metastatic BC (TransCONFIRM- TC). We showed that AP-2gamma is differentially expressed between responders and non-responders to Ful. The purpose of this study was to test the prognostic role of AP-2gamma by immuno-histochemistry (IHC) in the TC cohort and in a separate cohort of BC pts.

Material and methods: Nuclear AP-2gamma levels were evaluated by IHC on tissue microarrays of 124 primary BC samples from the TC cohort and in a separate cohort of primary BC from our institutional tissue bank. Hormone receptors, ki67 and HER2 status were reviewed centrally and pts classified for molecular subtypes according to the St. Gallen definition.

Results: In the TC cohort, 29% (15/51) of the luminal A, 62% (32/50) of the luminal B/HER2-neg, 90% (9/10) of the luminal B/HER2 +, 36% (4/11) of the triple negative and 100% (2/2) of the HER2 +, scored AP-2gamma positive. AP-2gamma positivity was more frequent in tumors with high grade (G3 76% vs G1 26%) or high ki67 (ki67 high 66% vs ki67 low 32%). Survival analysis of the entire TC cohort (n = 124) showed that AP-2gamma positive pts had a significantly shorter progression free survival (PFS) compared to negative patients [median (m)PFS AP-2gamma positive pts (n = 61): 5.4 months; mPFS AP2 negative pts (n = 63): 9.6 months; HR 1.082 (95% CI 1.013- 1.155) p 0.02]. A similar trend, not reaching statistical significance, was observed in a sub-analysis of the luminal population (n = 103; p 0.08). Results from our institutional tissue bank will be available at the meeting.

Conclusions: AP-2gamma is a prognostic factor for poor outcome in BC and pts with higher expressions of this marker in the primary tumor show poor outcome when treated with Ful in the metastatic setting. Mechanistic studies to dissect the role of AP-2gamma in endocrine resistance are warranted.

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