

30th Annual San Antonio Breast Cancer Symposium -- Abstract #5029

Estrogen receptor and breast cancer survival in a Kaiser permanente population-based study: comparison of quantitative reverse transcriptase polymerase chain reaction and immunohistochemistry.

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Background: Estrogen receptor (ER) status provides information on disease prognosis and response to endocrine therapy. We examined the associations between breast cancer survival and ER as measured by IHC (ER clone SP1) or by quantitative RT-PCR (Oncotype DX™ assay) in patients (pts) treated without and with tamoxifen (tam).

Subjects and Methods: Analyses were conducted in the Kaiser Oncotype DX case-control study population of node-negative breast cancer pts diagnosed from 1985-94 and not treated with chemotherapy (Habel et al, Breast Cancer Res 2006). Cases (n=220) were pts who died of breast cancer. Up to three controls (n=570) were matched to each case on age, race/ethnicity, tam therapy, diagnosis year and follow-up time. ER was assessed using standardized quantitative RT-PCR by Oncotype DX with the pre-defined cutoff for positivity of ≥ 6.5 CT units (each unit represents a 2-fold change in expression) and by a central lab using IHC (Cheung et al, JCO 2006), where pts with evaluable tumor tissue (94%) were categorized as negative (<1% nuclear staining = 0) or positive (semiquantitated as: 1-25%=1+; 25-75%=2+; >75%=3+). Conditional logistic regression was used to estimate the association between ER and risk of death. Analyses were stratified on tam therapy.

Results: Median age at diagnosis was 59 yr (range 28-74). 31% were tam-treated (mostly after 1988). For cases, the median time to death was 59 months (range 10-196). 84% of all pts were ER positive by IHC; 4% were 1+; 6% were 2+; 90% were 3+. By quantitative RT-PCR, 86% were ER positive; gene expression ranged from 2.9 to 14.1 C_T; median 10.5 C_T; 25% > 11.6 C_T. The overall concordance for ER status (positive vs. negative) by IHC and RT-PCR was 96%. In pts not treated with tam, those with 3+ values by IHC had a 60% lower risk of dying of breast cancer compared to those with 0 values (OR= 0.4, 95% CI= 0.3-0.7). By RT-PCR, those in the upper tertile of ER positivity were at 60% lower risk compared to ER negative pts (OR=0.4, 95%CI= 0.2-0.7). Among IHC ER+ tam-treated pts, a comparison across IHC values was not possible given the small numbers with 1+ or 2+ values. In contrast, in these same pts the risk of breast cancer death decreased with increasing ER expression by RT-PCR (OR= 1.0, 95%CI=0.4-2.3 and OR=0.4, 95%CI=0.2-1.0 comparing the lowest to the 2nd and 3rd tertiles).

Conclusion: Among ER+/ER- pts not treated with tam, ER by both IHC and RT-PCR was prognostic. ER by IHC was generally either very high or very low, whereas ER by RT-PCR was more continuously distributed with a large dynamic range. Among ER+

tam-treated pts, only quantitative RT-PCR using Oncotype DX allowed for a risk comparison across levels of ER expression and identified a 2.5-fold increase in survival for those with the highest quantitative ER expression.