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Background: Following the discovery of the homeobox 13 (HOXB13) to interleukin-17 B receptor (IL-17BR) expression ratio as a determinant of recurrence and death in tamoxifen treated women (Ma et al Cancer Cell 2004), we demonstrated that HOXB13/IL-17BR ratio was an independent predictor of breast cancer relapse and survival, but only in lymph node negative women (Goetz et al Clin Canc Res 2006). This finding was recently validated in a published cohort of 850 patients with ER positive, lymph node negative breast cancer (Ma et al J Clin Oncol 2006). In breast cancer cell lines, over-expression of HOXB13 is associated with increased invasion and migration (Ma et al Cancer Cell); however, the role of IL-17BR in breast cancer progression is unknown. Because IL-17 has been shown to inhibit tumor growth in mice through generation of specific cytolytic T lymphocytes (Benchetrit et al Blood 2002), and because lymphocytic tumor infiltration is associated with improved breast cancer outcome in some studies, we sought to determine whether the density of tumor infiltrating lymphocytes (TILs) differed with respect to the HOXB13/IL-17BR ratio.

Material and Methods: The HOXB13/IL-17BR ratio cut-point identifying patients at higher risk of breast cancer relapse and death was previously determined in a cohort of 130 ER positive, lymph node negative breast cancer patients treated in a prospective adjuvant tamoxifen trial (Goetz et al Clin Canc Res). 129 H and E slides were available, examined for TILs, and classified as none or minimal (grade 1), moderate (grade 2), or dense (grade 3) by the pathologist. The association between TILs and HOXB13/IL-17BR ratio was assessed using Fischer's exact test. Disease-free survival and overall survival were assessed with respect to TILs (grade 1 vs 2,3) using the logrank test and Cox pph models.

Results: TILs were assessed in 129 patients, and 89 (69%) were grade 1, 38 (29%) grade 2, and 2 (2%) grade 3. No significant association was found between presence of TILs (grade 1 vs 2,3) and the HOXB13/IL-17BR ratio (< vs > -1.339) (p=0.999). Additionally, neither disease-free survival (HR=0.77, 95%CI: 0.40-1.49, p=0.44) nor overall survival (HR=0.74, 95%CI: 0.32-1.53, p=0.42) differed with respect to the presence of TILs, (grades 2,3 relative to grade 1).

Discussion: The HOXB13/IL-17BR gene expression ratio, which identifies ER positive, lymph node negative breast cancer patients at higher risk of breast cancer relapse and death, is not associated with tumor infiltrating lymphocyte density in this tamoxifen treated breast cancer cohort.