00500 Poor Prognosis Associated With Hypoxia-inducible Factor 1-subunit Alpha (HIF1A) in Triple-negative Breast Cancer (TNBC) Can Be Mitigated by Androgen-receptor (AR) Expression and Adjuvant Anthracyclines

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Aims: Hypoxia-inducible Factor 1 (HIF1) is a master regulator of cellular responses to hypoxia and it has been shown that triple negative breast cancers (TNBC) display high HIF1A activity. Although HIF1A has been implicated in increased invasiveness, metastasis and treatment resistance in breast cancer patients in general, its role in TNBC prognosis has yet to be systematically studied. We aim to determine if HIF1A expression is a significant determinant in the prognosis of TNBC patients, and whether there are mitigating factors that can help direct therapeutic development for this subset of TNBC patients.

Methodology: Tissue microarrays (TMAs) were constructed from breast cancer tissues from 296 patients that were verified to have TNBC. Immunohistochemistry (IHC) was performed on the TMAs with antibodies against HIF1A and AR. HIF1a and AR positivity was defined as >1+ nuclear staining of tumor cells. Kaplan-Meier (KM) survival analysis was performed using SPSS and $p>0.05$ was considered as statistically significant.

Result: Out of 277 TNBC patients with valid IHC results, 129 (46.7%) were positive for HIF1A. KM survival analysis showed that AR expression rescued the relatively poor DFS in HIF1A+ patients [mean DFS: 116.5 months (HIF1A+/AR+) vs. 96.1 months (HIF1A+/AR-), $p=0.044$]. Interestingly, KM survival analysis also showed a trend towards poorer disease-free survival (DFS) in patients with HIF1A+ TNBCs [mean DFS=105.6 months (HIF1A-positive) vs. 117.4 months (HIF1A-negative), $p=0.19$]. Adjuvant treatment with anthracycline-based chemotherapy eliminated this trend [mean DFS: 123.9 months (HIF1A+) vs. 121.6 months (HIF1A-), $p=0.67$].

Conclusion: AR expression and anthracycline-based adjuvant chemotherapy improves DFS in HIF1A+ patients and ameliorates the poor prognosis. The results suggest that both AR and anthracyclines inhibit or modulate hypoxia-mediated pathways in TNBC. Interaction between AR and hypoxia in TNBC warrants further study.