Oral Abstract 28: Novel Hormone Receptor Positivity Cut-offs in Endometrial Cancer: A real-world Endometrial Cancer Molecularly Targeted Therapy Consortium cohort study

Presenting Author: Jessica Benally, MD, University of New Mexico

Topic
Endometrial

Objectives
While hormone receptor status is a known and commonly utilized prognostic marker in endometrial cancer, validated thresholds for estrogen (ER) and progesterone (PR) receptor are not well defined. We sought to describe the frequency of ER/PR related to other known prognostic factors and determine the optimal hormone receptor thresholds for progression-free survival.

Methods
A retrospective cohort study was conducted using the Endometrial Cancer Molecularly Targeted Therapy Consortium (ECMT2) database. Endometrial cancer patients with known ER/ PR status. Demographic and clinical characteristics were abstracted from the EMCT2 database. Unadjusted progression free survival (PFS) was estimated with the Kaplan-Meier method; log-rank tests were used to compare groups. Cox proportional hazards models with restricted cubic splines (RCS) were used to examine the functional association of ER or PR percent positivity with PFS. Bootstrap simulations with a Markov Chain Monte Carlo (MCMC) approach were used in the context of RCS to estimate thresholds.

Results
A total of 1631 patients were included. The proportion of ER+ (>1%) and PR+ (>1%) were 77.1% (n=1257) and 60.1% (n=981), respectively, and associated with lower grade and earlier stage ($p< 0.001$). The rate of ER positivity was higher in all ProMisE groups compared to PR positivity (dMMR 88.5% vs 76.4%; POLE mutated 79.5% vs 69.2%; p53abn 66.8% vs 43.4%; NSMP 81.2% vs 70.9%). Patients with ER positive status had a longer median PFS compared to patients who were ER negative (19.3 vs 12.7 months, $p< 0.001$). Similarly, patients with a PR positive status had a longer median PFS compared to those who were PR negative (19.8 vs 14.9 months, $p< 0.001$). RCS modeling demonstrated that positive expression exceeding 52% and 39% for ER and PR, respectively were associated with an improved PFS.

Conclusions
ER and PR were frequently expressed in endometrial cancer specimens and positively correlated with survival outcomes. Exploratory analyses identified optimal thresholds of 52% for ER and 39% for PR that are associated with superior PFS. Future research is needed to validate these candidate cut-points in independent cohorts and establish their predictive value for guiding antineoplastic therapy. We are grateful to The Kay Yow Cancer “Cancers that Affect Women" Fund in partnership with the V Foundation for Cancer Research for their generous support of the Endometrial Cancer Molecularly Targeted Therapy Consortium.

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