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5089 **Poster Session**

Early findings from the GARUDA trial: The impact of a genetic signature of late radiation toxicity on prostate cancer treatment decision making.

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Background: GARUDA (Germline DNA-Based Radiosensitivity Biomarker Influence on Toxicity Following Prostate Radiotherapy) was a single center phase II prospective study evaluating the impact of sharing results from a germline genetic signature (PROSTOX) characterizing patients as having a low or high risk of developing late $>$ 2 genitourinary (GU) toxicity from stereotactic body radiation therapy (SBRT) on decision making and toxicity. The goal of this early analysis was first to see if this information changed treatment choice, and second to see if patients categorized as genetically "low-risk" would have less late GU toxicity than those categorized as genetically "high-risk." **Methods:** PROSTOX is a test of germline mutations run in the MiraDx CLIA-certified laboratory. Results were reported to the ordering physician and their patient for joint decision-making before proceeding with treatment selection. To be enrolled on the study patients could choose SBRT or moderately hypofractionated radiation therapy (MHFRT) for treatment of their prostate cancer. 279 men were screened for the GARUDA study between November 2020 and May of 2022. 71 withdrew for a variety of reasons, primarily choosing another location for treatment or form of treatment. 208 patients remained on the protocol and are included in this exploratory analysis. Statistical comparisons of stratified proportions are based on Gaussian approximations to Binomial probabilities. **Results:** The average age for the cohort was 72.12 with the majority being non-Hispanic and Caucasian. Overall, 85.15% (177) of patients were classified as low-risk and 14.9% of patients (31) were classified as high-risk for late grade $>$ 2 GU toxicity by PROSTOX. There was not a significant difference in predicted toxicity risk by age (72.45 vs 70.2), ethnicity or race. Regarding treatment choice based on toxicity score, in patients determined to be low-risk, 1.2% chose MHFRT, and 98.8% chose MRI- or CT-guided SBRT. In patients who were classified as high-risk, 44.8% chose MHFRT, and 55.2% chose MRI- or CT-guided SBRT. The difference in treatment choice was significant ($p < 0.001$). In an early analysis of physician scored late $>$ 2 GU toxicity in patients with $>$ 18 months of follow-up ($n = 57$), 8.8% of patients had toxicity - 4.8% of those predicted to be low-risk, and 27.3% of those predicted to be high-risk ($p = 0.015$). **Conclusions:** In this exploratory analysis, predicting toxicity risk with PROSTOX significantly impacted patient and physician radiation treatment choice in localized prostate cancer. Early results also suggest that these changed treatment decisions lowered overall toxicity, which remained significantly different between patients classified as low-risk and high-risk. Analysis is ongoing to include patient reported outcomes and toxicity rates depending on treatment choice for those identified as high-risk. Clinical trial information: NCT04624256. Research Sponsor: U.S. National Institutes of Health.

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