615 THE IMPACT OF GENDER INCLUDING FEMALE MENOPAUSAL STATUS ON THE SAFETY AND EFFICACY OF IMMUNE CHECKPOINT INHIBITORS

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Background Estrogen and progesterone influence the immune system and thus may also influence clinical outcomes for patients (pts) with cancer receiving immune checkpoint inhibitor (ICI) therapy. Hence, we investigated if gender, premenopausal (PREMENO), and postmenopausal (POSTMENO) female states influenced ICI-associated clinical outcomes.

Methods In our multicenter study based on real-world data, we identified pts receiving anti-PD-1 or anti-PD-L1 [PD(L)-1] ICI monotherapy between 1/2011 to 4/2018 with follow-up until 1/2021 using pharmacy records. Immune-related adverse events (irAEs) by CTCAE V4.03, and physician-assessed tumor responses and time to treatment failure (TTF) were collected. Women under the age of 55 years were considered PREMENO following the World Health Organization's suggested average menopausal age.[1] We further investigated the non-small cell lung cancer (NSCLC) cohort receiving PD(L)-1 ICI in the metastatic setting for ICI efficacy analysis. Univariate analysis, multivariable logistic regression models, and Kaplan-Meier analyses were used to assess differences between male vs. PREMENO vs. POSTMENO.

Results We identified 913 pts receiving PD(L)-1 ICI: 58% (n=528) nivolumab, 35% (320) pembrolizumab, 5% (47) atezolizumab, and 2% (18) others. The median age for the entire cohort (EC) was 68 years, 56% (514) were male, 36% (328) POSTMENO, 7% (67) PREMENO, 65% (591) White, and 21% (192) African American. The most common tumor types were NSCLC and melanoma in 46% (417) and 12% (109), respectively. Any grade and grade $\geq$3 irAEs were 32% (290) and 8% (76) for the EC. No difference among POSTMENO vs. PREMENO vs. male was noted for overall survival (OS) (p=0.2) or TTF (p=0.2). Similarly, no difference in any grade irAEs was noted among the study cohorts (p=0.24). Among 393 pts with NSCLC, 51% (202) were male, 44% (171) POSTMENO, and 5% (20) PREMENO. The NSCLC group consisted of 60% (239) White, 28% (109) African American, 15% (60) with a history of autoimmune disease, and 33% (128) with <2 sites of metastasis. Again, no difference in OS (p=0.6) or TTF (p=0.8) was observed among the three NSCLC study cohorts. Any grade irAEs were noted in 30% (115) and grade $\geq$3 irAEs in 7% of NSCLC patients (28). No difference in any grade irAEs was noted for the three NSCLC study cohorts (p=0.12).

Conclusions In our study, gender, including female menopausal status, did not influence ICI safety or efficacy outcomes. While these findings are reassuring, further prospective studies, including pts with diverse cancer types and additional ICI regimens, are needed to universalize these findings.

Ethics Approval This study was approved by the Georgetown University Medical Center Institutional Review Board; approval number MODCR00002093

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