Poster #449P: Homologous Recombination Repair Gene Mutations Predict the Efficacy of Immune Checkpoint Inhibitors Therapy in Colorectal Cancer

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Background

- Homologous recombination repair (HRR) genes were known to predict response to immune checkpoint inhibitors (ICI) therapy in patients with advanced non-small cell lung cancer. However, whether HRR mutations are robustly predictive of a clinical benefit of ICI therapy for colorectal cancer (CRC) patients is not clear.

Methods

- A cohort treated with ICI from Memorial Sloan Kettering Cancer Center (MSKCC ICI cohort) was used to analyze the predictive value of HRR mutations on ICI therapy. The genomic data of The Cancer Genome Atlas (TCGA) dataset was used to analyze the correlation of the HRR mutations with immunogenic markers.

Results

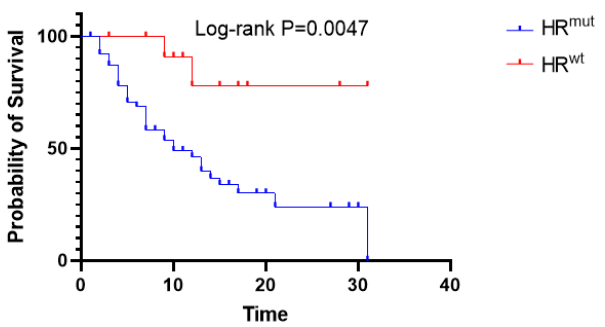

Figure 1. Kaplan-Meier survival curves of overall survival (OS) in MSKCC ICI cohort. HRwt, HRR wild-type; HRmut, HRR mutation.

- The HRR genes were commonly mutated (35.48%) in the pan-cancer TCGA cohort, with the frequency of 52.79% in CRCs.
- The CRC patients with HRR mutations had significantly improved overall survival (OS) than the patients without HRR mutations (hazard ratio (HR) =0.17, 95%CI 0.04−0.69, P=0.0047, Figure 1).
- There was no significant associations were identified in the TCGA colorectal adenocarcinoma (COADREAD) cohort of HRR mutations and survival (P=0.192, Figure 2), suggested that HRR alteration status was not a prognostic factor for CRC.

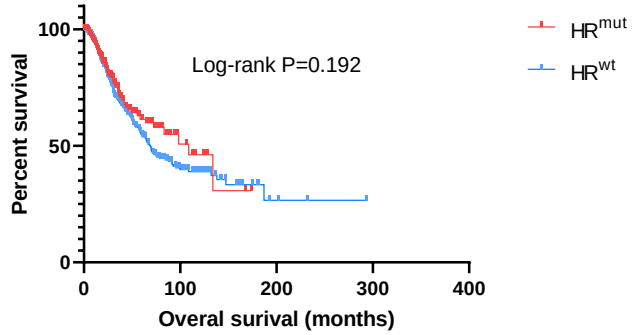

Figure2. Kaplan-Meier survival curves of overall survival (OS) in TCGA CRC cohort. HRwt, HRR wild-type; HRmut, HRR mutation.

Conclusion

- HRR mutations may serve as a positive predictor of ICI therapy in patients with CRC and their clinical value warrants further investigation.

Results

- HRR mutations were associated with higher tumor mutational burden (TMB) levels (P=0.011, Figure 3A), higher neoantigen levels (P=0.027, Figure 3B), increased CD8+ T-cell infiltration (P=0.036, Figure 4) and immune checkpoint molecule expression in the TCGA COADREAD dataset.

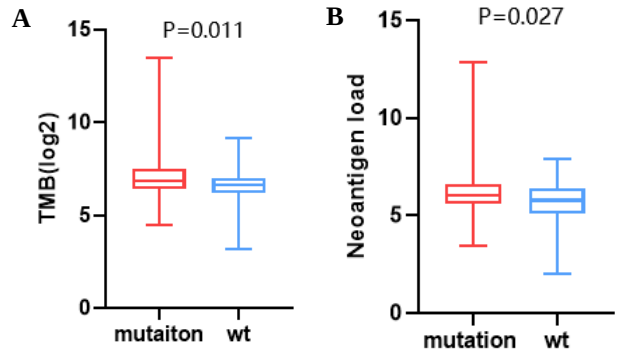

Figure 3. TMB(A) and neoantigen (B) distribution in cases with CRC in HRR mutation and wild-type group.

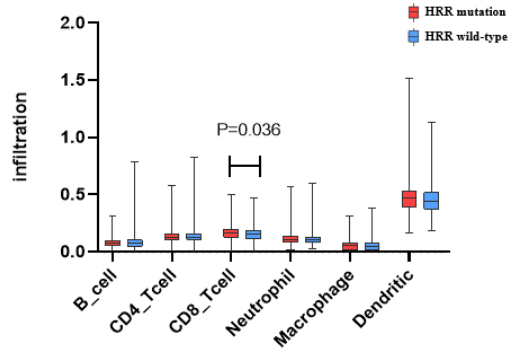

Figure 4. Immune cell subsets between HRR mutation and wild-type group.