INTRODUCTION

In colorectal cancers, characteristics of the tumor immune microenvironment (TIME) carry valuable implications for treatment resistance and/or response to immunotherapies. We have previously reported significant differences between the TIMEs of primary colorectal cancer (CRC-P) and CRC samples from various metastatic sites. Increased immune cell infiltration, B-cells, and CD8 cells, and decreased macrophages, were noted in CRC-P and lung metastatic (LuM) lesions compared to liver (LM) and peritoneum (PM) metastases.

Here, we expanded our work to microsatellite instability-high (MSI-H) CRC and compared their TIME to respective microsatellite-stable (MSS) tumor sites.

METHODS

• De-identified cases of MSS (n=6,732) and MSI-H (n=208) metastatic CRC that underwent next-generation sequencing with the Tempus Tx assay were selected from the Tempus Database.

• Gene expression patterns of immune cells, including B, T (CD4+, CD8+), NK cells, and macrophages, were used to predict relative intra-tumor abundance.

• MSI-H and MSS cohorts included CRC-P, LM, and PM. LuM was analyzed only in MSS tumors due to the limited number of MSI-H LuM. There was not a sufficient number of MSI-H Lung metastasis (n=5) to include in the analysis.

• Tumor mutational burden (TMB), neoantigen burden, and proportion of immune cells in CRC-P, LM, and PM were compared across MSI-H and MSS patients.

• Chi-squared/Fisher’s exact tests or Kruskal-Wallis tests were used to assess statistical significance.

SUMMARY

• MSI LM and PM have a more favorable TIME than respective MSS metastases, explaining the discordance in response to checkpoint inhibitors (CPI) and reported CPI benefits in MSI cases across all metastatic sites.

• MSS LuM have a comparable TIME to MSI metastatic sites, explaining the recently reported benefits from CPI therapy in this group.

RESULTS

Figure 1. TMB and Neoantigen Burden Across Primary and Metastatic Sites of MSI-H Patients

Figure 2. TMB and Neoantigen Burden between MSI-H and MSS Primary and Metastatic sites

Figure 3. TIME Comparison Between MSS and MSI-H Primary and Metastatic Sites

Figure 4. Comparison of MSS Lung metastases TIME with MSI-H Liver and Peritoneal Metastases