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DEEP, DURABLE RESPONSE TO PD-1 INHIBITOR MONOTHERAPY IN MICROSATELLITE-STABLE, TUMOR MUTATIONAL BURDEN-HIGH COLORECTAL CANCER

¹Samuel Schellenberg*, ²Leeseul Kim, ¹Young Kwang Chae. ¹Northwestern University Feinberg School of Medicine, Chicago, IL, United States; ²AMITA Health Saint Francis Hospital, Chicago, IL, United States

Background Immune checkpoint inhibitors have revolutionized care for a number of different cancer types. For colorectal cancer (CRC), a leading cause of cancer-related death in the United States, programmed cell death protein 1 (PD-1) inhibition is a treatment option for certain subsets of patients. High microsatellite instability (MSI-H) tumors are immunogenic, and thus PD-1 inhibition is first-line treatment. Anti-PD-1 therapy is generally not utilized for microsatellite stable (MSS) patients. Tumor mutational burden (TMB) is another predictive biomarker for immunotherapy response in all solid tumors. Here we present the case of a patient with MSS, TMB-H CRC resistant to multiple lines of chemotherapy, who responded to anti-PD-1 monotherapy.

Methods Case presentation.

Results A 64-year-old man with a family history significant for colon cancer was diagnosed with colorectal cancer, revealed to be moderately differentiated mucinous adenocarcinoma (stage IIIC) on biopsy. A tissue-based comprehensive genomic profiling of the cancer showed KRASG12D and ERBB2 amplification, microsatellite-stable, and TMB of 11mut/mB (FoundationOne). The patient progressed on multiple lines of therapy with multiple metastatic sites, and was briefly put under home hospice with diffuse abdominal pain and weight loss. The patient was started on pembrolizumab monotherapy, around 3.5 years after initial presentation. After five months on pembrolizumab, imaging showed significant improvement in pulmonary, hepatic, adrenal, and retroperitoneal metastases and the patient demonstrated partial response to treatment according to RECIST 1.1 criteria. The patient's carcinoembryonic antigen (CEA) levels had decreased from 45 ng/mL at treatment initiation to 2.8 ng/mL, and ctDNA analysis showed a blood TMB decrease from 31.58 mut/mB at treatment initiation to .96 mut/mB (figure 1), accompanied by decreases in the variant allele frequencies of the five most prevalent variants at the time of treatment initiation (Guardant 360). The patient's pain had nearly resolved by this point and pain medications were tapered off.

Abstract 631 Figure 1 Carcinoembryonic antigen (CEA) and blood tumor mutational burden (TMB) levels through six cycles of treatment with pembrolizumab

Conclusions This case demonstrates the existence of a subset of CRC patients who are MSS but TMB-H and may respond to immune checkpoint blockade. Comprehensive genomic profiling must be utilized in order to not miss this subset of patients. The mechanism of response in this subset of patients is unknown but warrants further exploration. Further studies should clarify the mechanism and likelihood of response to immunotherapy in MSS, TMB-H CRC patients, as this is critical to providing effective treatment for this subset.

Consent Written informed consent was obtained from the patient for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

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