A Case of Using Larotrectinib for NTRK Fusion-Positive Colon Cancer with Microsatellite Instability

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Introduction: NTRK gene fusion is a promising tumor-agnostic target and is known to be positive in about 0.3% of all types of cancer. Larotrectinib, a highly selective TRK inhibitor, has shown an overall response rate of 83% across various cancer types, making it an effective therapeutic agent for NTRK fusion-positive solid cancers. In this report, we present a case of using larotrectinib in a patient with colon cancer exhibiting microsatellite instability and harboring NTRK fusion.

Case Report: A 50-year-old female was diagnosed with ascending colon cancer, along with confirmed metastatic peritoneal seeding nodules and liver metastasis. Mutational studies revealed wild-type RAS, and negative BRAF V600E. MSI status was high. The patient received FOLFIRI with cetuximab, pembrolizumab, and FOLFOX with bevacizumab. However, disease progression occurred in the liver metastasis, and with limited remaining treatment options, NGS results revealed the presence of NTRK fusion. Subsequently, larotrectinib was administered, resulting in decreasing stable disease (-24%) with progression free survival (PFS) of 5 months.

Discussion: The application of targeted therapy, excluding cetuximab and bevacizumab, in colorectal cancer (CRC) is very limited. The detection of NTRK fusion in metastatic CRC is also very rare, accounting for less than 1% of cases. However, it has been relatively more frequent, around 5%, in MSI-high CRC, compared to approximately 0.4% in MSS CRC. Regorafenib and trifluridine/tipiracil are available options in patients who have been previously treated with fluoropyrimidine, oxaliplatin and irinotecan, but median PFS were 2.0 and 3.2 months, respectively. Therefore, efforts to identify NTRK fusion through genetic testing like NGS in CRC including MSI-H are crucial to obtain effective additional treatment options. In our case, the identification of NTRK fusion in an MSI-high CRC patient who had failed standard treatment allowed for the successful application of effective supplementary therapy.

Conclusion: NTRK fusion in CRC can be a significant treatment target, highlighting the importance of efforts to identify it for potential therapeutic benefits.