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Non-V600 BRAF mutations define a distinct molecular subtype of metastatic colorectal cancer

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Background: Molecular diagnostic testing has become an integral part of the evaluation of patients with metastatic colorectal cancer (CRC). However, expanded mutational testing often identifies mutations with unclear clinical, therapeutic or prognostic implications. One such example is *BRAF* mutations which occur outside of codon 600 (non-V600*BRAF* mutations).

Methods: We completed this multicenter, retrospective cohort study to fully characterize the clinical, pathologic and survival implications of non-V600*BRAF* mutations in metastatic CRC. We identified and pooled all patients with CRC in whom non-V600*BRAF* mutations were identified from NGS databases at three large molecular genetics reference labs.

Findings: A total of 9643 patients with metastatic CRC underwent NGS testing. We identified 208 patients with non-V600*BRAF* mutations, which accounted for 21.5% of all *BRAF* mutations. The estimated prevalence of non-V600*BRAF* mutations in all patients tested was 2.2%. Cancers with non-V600*BRAF* compared with V600E*BRAF* mutations were found in patients who were significantly younger (58 vs. 68 years; p<0.0001), less likely to be female (46% vs. 65%; p=0.0008), and had less high grade (13% vs. 64%; p<0.0001), or right-sided primary tumors (36% vs. 81%; p<0.0001). Median overall survival (OS) was significantly longer in patients with non-V600*BRAF* mutations compared to those with V600E*BRAF*-mutant metastatic CRC (OS: 60.7 months vs. 11.4 months; p<0.0001). In multivariate analysis, non-V600*BRAF* mutation remained independently associated with improved OS (HR: 0.18; p< 0.0001).

Interpretation: Non-V600*BRAF* mutations occur in approximately 2.2% of patients with metastatic CRC and define a new subtype of CRC with an excellent prognosis.

Biography

Humaid Al-Shamsi is currently working as an Assistant Professor, University of Texas MD Anderson Cancer Center and he is also positioned as an Assistant Clinical Professor (Part Time) in the Department of Oncology at McMaster University. He has been a recipient of many awards and grants. His research experience includes various programs, contributions and participation at different countries for diverse fields of study. His research interests reflect in his wide range of publications in various national and international journals. His research interests include Oncology, Radialogy, Hepatology, Clinical Oncology, etc.

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