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ABSTRACT

Clinical Significance of KRAS Mutation in Colorectal Cancer (CRC) Patients.

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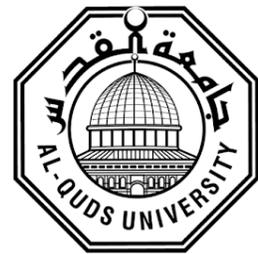
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Background: According to 2018 Palestinian statistics, CRC is the second most common type of cancer; it contributes significantly to cancer-related deaths despite the continuous progress in diagnostic and therapeutic methods. One of the advances in CRC is the introduction of EGFRi that increased the treatment options available for a patient with mCRC, two EGFRi agents are approved for the treatment of mCRC: panitumab and cetuximab.

KRAS is the most frequently mutated oncogene in cancer. KRAS gene mutation in CRC is a well-established biomarker for predicting tumor responsiveness towards the use of EGFRi. KRAS gene mutation is available at Palestinian MOH, testing started in 8/2019 for patients at Stage 4 metastatic CRC (because in Stage 1 to 3 even if KRAS mutation was positive this did not result in a change in therapeutic regimen).

Oncologists can make the clinical decision regarding therapy according to KRAS test results, where if the result shows wild type KRAS, the therapy is Avastin and/or EGFRi. However, patients with mutant KRAS, EGFRi are known to be not effective. So, all metastatic CRC patients must undergo genetic testing to differentiate between the wild type and mutant KRAS in order to avoid side effects of EGFRi and save drug cost.

Objectives: Compare outcome between lab testing results and patient records in order to determine if the input provided from the lab is implemented in patient treatment protocol and to



evaluate if international treatment protocols are being implemented in a colon cancer patient with KRAS mutation.

Methods: The study involved 88 patients diagnosed with CRC and treated between 2016-2020 in Beit Jala, Alwatani, Refedia and Thabit Hospitals. 40 patients had genetics analysis in the national blood bank Ramallah- Palestine.

Results: A total of 88 CRC patients were included in the study, 45 were female, 43 were male. 37.5% of patients were above 60 years old. The study included a random sample of 48 CRC patients, 29/48 (60.42%) received chemotherapy, 6/48 (12.5%) received biological (Avastin) and chemotherapy 8/48 (16.66%) underwent radiotherapy and 29/48 (60.42%) underwent surgery. Out of the 48 randomized CRC patients, 16/48 (33.33%) had metastasis.

Out of the 88 CRC patients, 40 had KRAS gene test results, 27 (67.5%) were found to have KRAS mutation; all are Stage 4 metastatic (32.5% metastasis to the liver). 33 patients underwent therapy, 11 of them had wild type KRAS while 22 had mutant KRAS. All treated patients received chemotherapy, 9 of them (27.27%) underwent surgery; 3 (9.09%) underwent radiotherapy. Biological drugs were administered to 21 (63.63%) patients, 7 of them had wild type KRAS (2 patients received bevacizumab (Avastin[®]), 4 patients received cetuximab and 1 received trasuzumab). The remaining 14 patients had mutant KRAS, 13 patients of them receive Avastin and 1 patient received cetuximab with chemotherapy.

Conclusions: The introduction of KRAS mutation test at Palestinian MOH is an important advance in mCRC treatment that can directly influence medical decision-making and selection of the appropriate biological treatment. The data collected also indicates that a high percentage (67.5%) of mCRC Palestinian patients have mutant KRAS.

Key words: Colorectal cancer, biomarker, wild and mutant KRAS, Biological therapy, EGFR, Avastin