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Commentary

on Encorafenib plus cetuximab in patients with BRAF^{V600E}-mutated metastatic colorectal cancer — Polish multicenter experience

Advanced colorectal cancer (CRC) with a *BRAF* gene mutation is a complex and serious medical problem. *BRAF* mutations are classified based on their functional significance in the mitogen-activated protein kinase signaling pathway. The most common is *BRAF^{V600E}* mutation, which results in pathway activity independently of the RAS kinase and is associated with a worse prognosis. *BRAF^{V600E}* mutated tumors are often associated with high mutational burden, microsatellite instability, and high levels of epigenetic modulation of gene expression through DNA methylation.

Treatment of patients with advanced CRC with the *BRAF^{V600E}* mutation is an unmet need, mainly due to unfavorable prognosis and limited targeted treatment options.

Based on the results of clinical trials, a treatment paradigm has been established, which includes first-line chemotherapy with bevacizumab and, in case of failure, a combination of inhibitors of mutant BRAF kinase and epidermal growth factor receptor (EGFR). The BEACON trial provided evidence of improved survival in patients receiving the combination of these drugs, encorafenib and cetuximab.

Further efforts are aimed at assessing the value of this combination in first-line treatment, as well as in the treatment of earlier stages of disease. Ongoing preclinical and clinical trials are also examining combinations of encorafenib and cetuximab with immunotherapy and chemotherapy. Another subject of research is also the mechanisms of adaptive and acquired resistance to both drugs.

In this issue readers can read the paper assessing the experience of Polish oncologists in the use of encorafenib with cetuximab in patients with advanced CRC with the *BRAF^{V600E}* mutation.

The specific conditions of financing such treatment from public sources limit its wide application. However, taking into account the profile of the disease and its aggressive course, such treatment should be considered in every patient with this particular molecular disorder, also in second-line treatment.

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