STRESZCZENIE W JĘZYKU ANGIELSKIM

Treatment of metastatic colorectal cancer (mCRC) for many years was based primarily on the use of systemic chemotherapy. Better understanding of the molecular biology of this disease led to the introduction of molecular targeted therapy. Currently, the assessment of the presence of mutations in the *KRAS, NRAS* and *BRAF* genes is mandatory for the qualification of mCRC patients for treatment with monoclonal antibodies against EGFR. The literature data indicate that mutation in *RAS* genes occurs in approximately 45-50% of patients, *BRAF* in approximately 10% of patients, and *PIK3CA* in approximately 40% of mCRC patients. Contemporary mCRC treatment algorithms incorporate the use of anti-EGFR antibodies - cetuximab and panitumumab. However, those drugs are effective only in selected patients with colorectal cancer. Patients with a mutation in *KRAS, NRAS* and *BRAF* genes should not be treated with anti-EGFR monoclonal antibodies, because they do not derive any clinical benefit from such therapy. In this particular group of patients treatment with anti-EGFR therapy may result in a shortening of survival. Furthermore, patients may experience significant treatment-related toxicity.

Hence, defining predictive as well as prognostic factors for anti-EGFR therapy may an important goal for many medical and socio-economic reasons.

Accordingly, in this study the predictive value and prognostic value of mutations in *RAS (KRAS, NRAS), BRAF* and *PI3KCA* genes have been assessed in patients with stage IV colorectal cancer treated with anti-EGFR monoclonal antibodies. The association of the above-mentioned parameters with the survival time of patients with advanced colorectal cancer and on the percentage of objective responses were analyzed.

The analysis included 110 patients who underwent anti-EGFR therapy in the Bialystok Center of Oncology (BCO) in 2006-2014. *RAS* gene (*KRAS, NRAS*),

BRAF and *PIK3CA* genes mutation assays and medical history data have been analyzed to create a database of clinic-laboratory parameters. The aforementioned variables have been correlated with patients' 1-year survival time, clinical and laboratory data, such as: location of the primary change (left-side vs right-site), general fitness status according to WHO, stage of T-tumor to TNM classification, presence and number of distant metastases, degree the severity of skin toxicity during anti-EGFR therapy, the level of leukocytosis, neutrophils, lymphocytosis, hemoglobin, platelets, NLR, PLR and CRP.

It was demonstrated that the occurrence of mutations in exons 3 and 4 of the *KRAS* gene and 2, 3, 4 of the *NRAS* gene and in exon 15 of *BRAF* gene are negative predictive factors of the response to treatment with anti-EGFR monoclonal antibodies.

The need to consider the *PIK3CA* gene status has been confirmed before initiating treatment with anti-EGFR antibodies.

The absence of distant metastases and the low clinical stage of the tumor (T – tumor to TNM classification) showed features of favorable prognostic factors.

The occurrence of severity of skin toxicity in patients with mCRC treated with EGFR inhibitors is a predictor of survival and disease progression.

It has been shown that patients with left-sided tumor have better responses to anti-EGFR treatment compared to patients with right-sided mCRC.

There was no correlation between age, gender, performance status prior to treatment initiation and overall survival.