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Detection of clinically significant gene variants in colon adenocarcinoma samples of ukrainian patients using a cancer hotspot panel

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Colon cancer, one of the most common type of cancer in developed countries, was analyzed to identify clinically relevant gene variants in the samples from Ukrainian patients. **Methods.** The study included 74 samples from the patients aged 60–87 years, all from the Ukraine, who had colorectal cancer of various localization and differentiation degree. They were collected in accordance with the requirements of the Helsinki Declaration, agreements with medical institutions and approvals of their Ethics Committees. Next-generation sequencing (NGS) was performed on an IonS5 Plus instrument (ThermoFisher Scientific) with a Cancer Hotspot Panel (CHP). The results were then filtered using the Franklin by Gennox according to clinical classifications. **Results.** A total of 244 cases of clinically significant and potential clinical relevant altered gene variants (Tier 1–3) were found in 36 of 50 genes of 67 colon cancer samples. Two types of genetic changes were identified: SNVs and INDELs. SNPs cover more than 85% of the detected genetic changes. According to the ACMG Classification about 55% of identified clinically significant gene variant`s cases were determined as Pathogenic. 31% of cases of identified mutations were characterized as Likely pathogenic and more than 30% of cases of mutations were determined as Uncertain. More than 25% of cases classified to Tier 1 in 45 samples, which are the most clinically significant, and more than 30% of total cases were referred to the Tier 2 group of mutations in 51 samples. Somatic and likely somatic gene variants (VAF < 30%) accounted for more than 70%. Tier 1–2 gene variant cases were detected for the *BRAF, KRAS, NRAS, PIK3CA, AKT1, APC, ATM, ERBB2, FBXW7, IDH1, PTEN, SMAD4, TP53, VHL*. The largest number of Tier 1–2 mutation spectrum was found in the genes: *KRAS, PIK3CA, APC, TP53, BRAF, NRAS, FBXW7,* and *SMAD4.* All *KRAS* mutations belong to Tier 1 and are the so-called hot spots in the p.Gly12–13 positions of the protein (c35G and c38G). The hotspot mutations with Tier 1 were detected for *PIK3CA* in p.Glu542 (c.1624G), p.Glu545 (c.1633G), p.Arg88 (c.263G), p.His1047 (c.3140A) *etc.* The *BRAF* gene Tier 1 mutations were p.Val600 (c.1799T). These genetic alterations have the highest significance for colon cancer in diagnostic, prognostic, and therapeutic implications. As for the numerous Tier 3 group of mutations (more than 100 cases in 28 genes), additional studies are needed to prove their clinical significance. **Conclusions.** The data demonstrate the high level identification of the clinical significant gene variants in the colon cancer samples by the CHP. Further confirmation on a larger number of samples and deeper analysis of clinical significant gene variants as potential clinical relevant mutations by other approaches would be beneficial.

Keywords: NGS, clinically significant gene variants, Cancer Hotspot panel, colon cancer.