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Evaluation of KRAS Mutational Status in Pancreatic Ductal Adenocarcinoma

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ABSTRACT

Pancreatic ductal adenocarcinoma (PDAC) is one of the most lethal malignancies with a dismal prognostic. KRAS is a well-recognized driver gene in PDAC, detected in the earliest stages of pancreatic tumor transformation. To establish the frequency of KRAS mutations in a cohort of Romanian patients, we performed Sanger sequencing for exon 2 and exon 3 of the gene on 31 PDACs pairs. We further examined correlation of the mutational status with clinico-pathologic data of the patients and evaluated the prognostic implication of KRAS mutations. Ten out of 31 patients (32%) had KRAS missense mutations, all were detected in exon 2, and codon 12 only. Among patients with KRAS mutations, the majority (7/10, 70%) had c.35G>A (p.G12D) substitutions. Patients with p.G12D mutations had a marginally worse survival (p=0.07) and a shorter disease-free survival (p=0.04) when compared to KRAS wild-type patients. Correlation between patients age and recurrence was seen in KRAS wild-type cohort (p=0.096, r=-0.6). In summary, evaluation of KRAS mutational status is a predictor for PDAC patients` prognosis and further KRAS directed therapy might prove to be an efficient tool in patients having KRAS mutations.

Key words: pancreatic ductal adenocarcinoma, Sanger sequencing