

The spectrum of mutations in BRCA1/2 detected by NGS in pancreatic cancer patients considered for treatment with PARP inhibitor.

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Introduction

Mutations in the BRCA1/2 genes are responsible for hereditary breast cancer, ovarian cancer, prostate cancer as well as pancreatic cancer. The results of pancreatic cancer treatment are still unsatisfactory with a five-year survival rate of only 8.8% (KRN) in Poland (11% in the US). Recently, PARP inhibitors have been introduced as a promising treatment option for pancreatic cancer patients with mutations in the BRCA1/2 genes.

Aim

The purpose of this study is to review the spectrum of detected mutations in BRCA1/2 genes in patients referred for molecular diagnosis due to consideration of PARPi treatment.

Material and Methods

Between 2020 and 2022, 143 patients with stage III and IV pancreatic cancer were tested for BRCA1/2 genes by NGS in DNA isolated from 116 (82%) blood samples and 28 (18%) cancer tissue samples.

Results

In 3/28 (11%) tissue samples showed DNA degradation and no test result was obtained. No mutations in BRCA1/2 were detected in any of the tissue samples tested. All 8 pathogenic mutations were detected in blood samples. Two mutations were detected in the BRCA1 gene and six in BRCA2. In total, mutations were detected in 5.7% (8/140) of the patients studied.

Conclusions

BRCA1/2 diagnosis for pancreatic cancer should be carried out by NGS because the mutations are mostly confined to the BRCA2 gene and additionally scattered throughout the gene. In one case, founder mutation were detected in the BRCA1 gene.