doi.org/10.51219/URForum.2021.Tatiana Zavarykina

UNITED RESEARCH FORUM
(CONNECT WITH RESEARCH WORLD)

2nd International E-Conference on

CANCER SCIENCE AND THERAPY

August 23-24, 2021 I Webinar

Molecular Genetic Markers and Relapse of Ovarian Cancer After Platinum-Based Chemotherapy

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The most important aim of the modern clinical oncology is the personalized treatment of cancer patients. The key drugs used in chemotherapy of ovarian cancer are platinum derivatives, so it makes relevant to search for sensitivity markers to this group of drugs. We investigated the association of polymorphic markers of DNA repair genes *XRCC1, ERCC2, XPG (ERCC5)*, the cell cycle regulation genes *TP53, MDM2, CDKN1A*, gene of transport protein ABCB1, frequent mutations of *BRCA1* gene, and methylation of four genes *(BRCA1, RASSF1A, DAPK1, GSTP1)*. We evaluated the median progression-free survival time (PFS) and the risk of relapse for all studied markers. PFS is a surrogate clinical marker of sensitivity of ovarian cancer to platinum drugs. The most important results were obtained for marker Gln399Arg of XRCC1 (p=0.025) during the follow-up period up to 19 months from the end of chemotherapy, mutation 5382insC (p=0.035) and inactivation of BRCA1 gene function by promoter methylation or the presence of the C/C genotype (p=0.033). Trends to significance were observed for markers *Arg72Pro* of *TP53, Ser31Arg* of *CDKN1A, T(-410)G* of *MDM2*, promotor methylation of *BRCA1, RASSF1A, GSTP1*, and for methylation of at least one of the four studied genes *(BRCA1, RASSF1A, DAPK1 и GSTP1)*. When a group was divided according to the type of surgery, a statistically significant associations with PFS for markers of genes *CDKN1A (p=0.01), TP53 (p=0.04), BRCA1 (p≤0.04)* were detected in subgroup with the complete and optimal debulking. Using multivariate data analysis, a model of risk of relapse during the follow-up period up to 19 months from the end of chemotherapy was obtained.

Keywords: Ovarian cancer, polymorphic marker, DNA methylation, progression-free survival, platinum-based chemotherapy

Biography:

Tatiana Zavarykina works in the Emanuel Institute of Biochemical Physics of Russian Academy of Science since 2002. In 2008 defended a Ph.D. thesis. From 2010 works in the molecular oncology field. From 2015 works on the project dedicated to the search for markers of sensitivity to platinum-based chemotherapyof ovarian cancer.

ISBN: 978-1-8382915-4-9