Clinical Outcome of BRCA1-associated Epithelial Ovarian Cancer: Significance of 4153delA and 5382insC Mutations

Grigorijs Plakhins [1, 2], *Arvids Irmejs* [1], *Gunta Purkalne* [1], *Genadijs Trofimovics* [1], *Edvins Miklasevics* [1], *Janis Gardovskis* [1]

[1] *Rīga Stradiņš University, Institute of Oncology, Latvia*
[2] *Daugavpils Regional Hospital, Daugavpils, Latvia*

Introduction. The impact of the mutations in the BRCA1 gene on the clinical outcome of epithelial ovarian cancer has been extensively investigated, and despite some conflicting results, most recently published studies have reported higher survival rates for BRCA1-associated ovarian cancer patients. Due to the genotype-phenotype correlation effect, carriers of BRCA1 mutations in different regions of the BRCA1 gene have different risks for developing breast and ovarian cancer. Moreover, breast cancer patients who are carriers of the 4153delA mutation have a poorer clinical outcome than carriers of the 5382insC mutation. However, the correlation of individual BRCA1 mutations with the survival rates of epithelial ovarian cancer patients has not yet been fully investigated.

Material and methods. Ovarian cancer patients carrying the three most prevalent BRCA1 mutations in Latvia (300T/G, 4153delA and 5382insC) were screened at the Institute of Oncology of Rīga Stradiņš University as part of a nationwide case-control study. Patients who were diagnosed with primary ovarian cancer from 2005–2011 and who underwent mutational analysis before or within 6 months following surgery were included in the study.

Results. Out of 196 patients, 91 had BRCA1 mutations: 4153delA (n = 45), 5382insC (n = 46). The mean estimated survival time was 41.6 months among carriers (36.4 and 46.4 months among 4153delA and 5382insC mutation carriers, respectively), and 36.1 months among non-carriers. The overall survival of the 5382insC mutation carriers was significantly better than both 4153delA mutation carriers (χ^2 = 4.09, DF = 1, p = 0.043) and non-carriers (χ^2 = 7.14, DF = 1, p = 0.008). The difference in overall survival between the 4153delA mutation carriers and non-carriers was not statistically significant. A multivariable analysis revealed that the 5382insC mutation remains an independent predictive factor of improved survival for epithelial ovarian cancer patients.

Conclusions. Specific mutations within the BRCA1 gene can have different impacts on the clinical outcome of epithelial ovarian cancer. Further clinical studies are needed to determine the significance of various ovarian cancer treatment options for carriers of individual BRCA1 mutations located in different parts of the BRCA1 gene.