

Every year more than two hundred thousand women in the world are diagnosed with ovarian cancer. In most cases, despite the use of radical surgical treatment combined with chemotherapy, the disease progresses and ends with death. Serous ovarian carcinoma is the most common type of the ovarian cancer, characterized by worse prognosis. Although the progress of molecular diagnostics has made it possible to better understand the biology of this tumor, it has not been found to improve the treatment.

The article published in 2012 indicated the occurrence of the abnormalities in the gene encoding the anaplastic lymphoma kinase (ALK) – protein that controls cell divisions and survival, in ovarian cancer. Such alterations in other cancers have often been associated with adverse prognosis, affected the treatment or could have even been considered the primary cause for cancer development. Moreover, there is a drug on the market from 2011 that in the specific manner targets the cancer cells that show the abnormal presence of ALK protein causing their death without damaging the healthy cells. The possibility to use such a therapy would be a breakthrough in the treatment of the advanced ovarian carcinoma.

Our main goal is to determine the type and incidence of the alterations of ALK encoding gene in the ovarian serous carcinoma from the Polish population, and to investigate the effect of these abnormalities on the survival (role as a so-called prognostic factor) and the response to the conventional therapy (role as a so-called predictive factor). To achieve this, a number of laboratory tests will be conducted on the material from the surgically treated patients. We will start by preparing the tissue microarrays containing the tissue samples from many tumors, which will allow for the simultaneous examination of multiple cases. Then the tissue microarrays will be sliced and immunohistochemically stained to determine if an excessive amount of ALK protein is present in the tumor. We will use three different kinds (clones) of the anti-ALK antibody to assess which of them is the most suitable for the identification of overproduction of ALK in ovarian carcinomas.

The next step is to conduct the more advanced molecular tests, namely fluorescent in situ hybridization and Sanger sequencing. The first method, in which a fluorescent probe binds to the ALK gene in the tumor cells, will allow us to determine if the gene fragments were not translocated to another chromosome, forming so-called fusion gene, and if the number of the gene copies is not increased, which is also important in the process of carcinogenesis. With the Sanger sequencing we will in turn be able to detect even the smallest changes within the gene sequence, the so-called point mutations.

The obtained results will be analyzed statistically and correlated with the observed survival and the used therapy to assess the predictive and prognostic role of the detected abnormalities. In addition we will evaluate if the immunohistochemistry results translate into the results of more expensive molecular tests, and therefore could be used as a screening method for the detection of ALK alterations. The development of such a diagnostic algorithm would in the future allow for the selection of patients who could benefit from the novel targeted anti-ALK therapy.

In conclusion, this study may allow a better understanding of the biology of the ovarian carcinoma and enable a more accurate determination of the prognosis and response to the classical treatment, as well as estimate the proportion of patients that could potentially benefit from the modern targeted therapy. Additionally it may also help to develop an effective diagnostic algorithm to facilitate the detection and assessment of the investigated abnormalities.