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Monitoring the cardiotoxic effects of poly (ADP) ribose polymerase inhibitors in patients with advanced ovarian cancer

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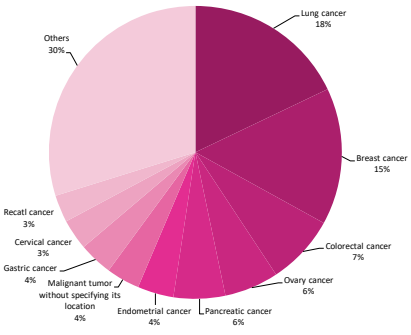
Introduction

One of the most common malignant neoplasms among women is ovarian cancer, which accounts for about 5% of all cases. In 2019, nearly 4,000 cases and about 3,000 deaths were diagnosed in Poland. Risk factors include carrier of BRCA1 or BRCA2 mutations, childlessness, multiple ovulations. Due to the high metastasis potential and the initially mildly symptomatic course, most diagnoses are made in stage III and IV. Consequently, in everyday clinical practice we have to deal with the problem of diagnosis and treatment. Treatment of ovarian cancer depends largely on the stage and histopathological type of the cancer, age and procreation plans of the patient. The mainstay of treatment is surgery as much as possible, followed by chemotherapy and radiotherapy. At the beginning of January 2022, new groups of drugs - olaparib and niraparib (PARP inhibitors) - used in the treatment of ovarian cancer, will be reimbursed. Standard chemotherapy for ovarian cancer includes the administration of carboplatin and paclitaxel - drugs with documented cardiotoxicity resulting from oxidative damage to cardiomyocyte structures. At the same time, it is known that activation of the enzyme poly (ADP) ribose polymerase in cell nuclei under oxidative stress conditions plays an important role in cell damage. Some studies suggest that the cardiotoxicity of doxorubicin (used in relapse) may be mediated indirectly by PARP activation. Therefore, drugs belonging to the group of poly (ADP) ribose polymerase inhibitors could reduce the cardiotoxicity of classical chemotherapy. However, there are reports suggesting that PARP inhibitors may cause cardiotoxicity, most often in the form of arterial hypertension. In one study, almost half of the patients treated with PARP inhibitors developed cardiovascular side effects [5]. However, the available data on the cardiotoxicity of PARP inhibitors are incomplete. The current available literature does not provide a complete picture of possible complications from the cardiovascular system.

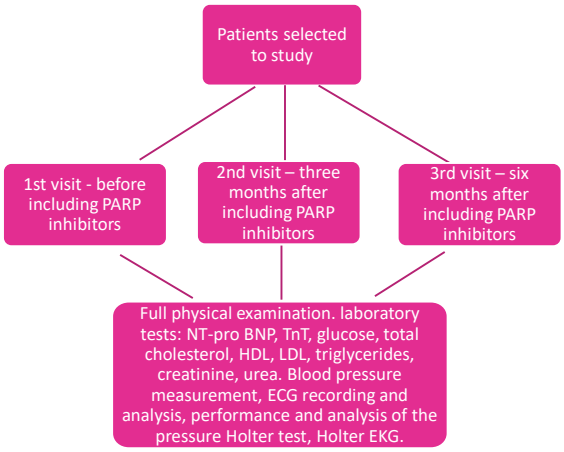
Main causes of cancer mortality in Poland, 2019



The aim of study

The main aim of the study is to assess the cardiotoxic effects of advanced ovarian cancer treatment with olaparib or niraparib.
The specific objectives are:
• Assessment of cardiac damage in patients with advanced ovarian cancer receiving olaparib or niraparib, using strain and strain rate imaging.
• Assessment of the risk of cardiovascular complications in patients treated with olaparib or niraparib, depending on pre-treatment cardiovascular risk factors.
• To evaluate the usefulness of the assessment of myocardial deformation and other echocardiographic parameters in the diagnosis of early and late cardiac complications in patients treated with olaparib or niraparib.
• To assess the risk of developing cardiac arrhythmias induced by olaparib or niraparib.
• To assess the risk of developing high blood pressure induced by olaparib or niraparib.
• To assess the risk of acute coronary syndrome induced by olaparib or niraparib.
• Assessment of the risk of pulmonary embolism induced by olaparib or niraparib.

Methodology



Expected results

The obtained results may be important in the context of the diagnosis of cardiac complications in patients treated with PARP inhibitors, because they are potentially cardiotoxic drugs and early detection of complications will allow for modification of treatment or early implementation of preventive strategies before the onset of full-blown heart failure. Heart failure, hypertension, arrhythmias may make it difficult or even impossible to treat cancer effectively. We expect some patients to develop hypertension. The use of strains will allow the detection of subtle abnormalities in the contractility of the heart muscle.

Actual results

So far, approximately 15% of the planned research group has been recruited. 40% of the patients have developed arterial hypertension. One person was disqualified from treatment due to life-threatening complications. The plans include expanding the research group and potentially establishing cooperation with another oncological center.

References

P. Pacher, L. Liaudet, P. Bai, L. Virag, J. G. Mabley, G. Haskó and C. Szabó. Epidemiology, Activation of Poly(ADP-Ribose) Polymerase Contributes to Development of Doxorubicin-Induced Heart Failure - Journal of Pharmacology and Experimental Therapeutics March 2002, 300 (3) 862-867; DOI: https://doi.org/10.1124/jpet.300.3.862.

M. Blanco Clemente, M. Martinez Cutillas, Y. Garitaonaindía Díaz, B. Menchen Viso, M. Provencio Pulla, C. Maximiano Alonso.749P Cardiotoxicity in patients treated with PARP-inhibitors. DOI:https://doi.org/10.1016/j.annonc.2021.08.1191.

Other activities

1. Active participation in the 4th Baltic Cardio-Oncology Meeting (November 26, 2022), Gdańsk - presentation of a case: "Acute heart failure in a patient with breast cancer treated with trastuzumab and pertuzumab.„
2. Publication of the article MTHFD1 c.1958G> A and TCN2 c.776G> C polymorphisms of folate metabolism genes and their implication for oral cavity cancer. Katarzyna Malinowska, Alicja Nowak-Zduńczyk, Anna Merecz-Sadowska, Anna Szczepańska, Dariusz Kaczmarczyk, Katarzyna Bliźniewska-Kowalska, Hanna Zielińska-Bliźniewska.