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219 EFFECT OF OLAPARIB TREATMENT ON CELL CYCLE, SENEESCENCE AND CELL DEATH IN OVARIAN CANCER CELLS

¹P Tudrej*, ²M Glowala-Kosińska, ³D Sojka, ⁴AJ Cortez, ³KM Lisowska. ¹Department of Genetic and Molecular Diagnostics of Cancer, Maria Skłodowska-Curie National Research Institute of Oncology, Poland; ²Department of Bone Marrow Transplantation and Hematology-Oncology, Maria Skłodowska-Curie National Research Institute of Oncology, Poland; ³Center for Translational Research and Molecular Biology of Cancer, Maria Skłodowska-Curie National Research Institute of Oncology, Poland; ⁴Department of Biostatistics and Bioinformatics, Maria Skłodowska-Curie National Research Institute of Oncology, Poland

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Objectives High-grade serous ovarian cancer (HGSOC) is the most frequent and deadly histological type of ovarian cancer. Targeted treatment approaches, such as PARP inhibitors, have brought significant improvement in management of this disease. Here we analyzed molecular mechanisms of olaparib influence on ovarian cancer cells.

Methods We used our newly established HGSOC cell line OVPA8 (ECACC #1906260¹) and three other lines (A2780, SKOV3, KURAMOCHI). BRCA1/2 mutations were analyzed by Sanger sequencing and NGS. Cells were treated by olaparib (AZD2281). Metabolic activity and viability were assessed using AlamarBlue and crystal violet assay, respectively. Half maximal inhibitory concentrations (IC50) were determined using GraphPadPrism software. Cell death and cell-cycle distribution were analyzed by flow cytometry.

Results NGS analysis revealed BRCA1 pathological mutation c.3700_3704delGTAAA (p.Val1234Glnf) and loss of heterozygosity in BRCA2 in OVPA8. BRCA2 pathological mutation c.6952C>T (p.Arg2318Ter) was described in KURAMOCHI, BRCA2 mutations of unknown significance in A2780 (c.T8195G, p.L2732X) and SKOV3 (c.7364A>G, p.H2455R).² The IC50 values were 3.99μM, 5.13μM, 6.77μM and 25.6μM for OVPA8, A2780, KURAMOCHI and SKOV3, respectively. Olaparib treatment resulted in G2/M arrest in all cell lines, increased senescence and cell death (except SKOV3).

Conclusions All analyzed cell lines, except SKOV3, had low olaparib IC50 values. The same correlation was found for the level of cell death and senescence what may be related to the functional status of BRCA1/2. Cell cycle G2/M phase arrest was observed in all ovarian cancer cell lines.

REFERENCES

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220 FUNCTIONAL ANALYSIS OF ZFH4 AS A NOVEL THERAPEUTIC TARGET IN OVARIAN CANCER

Y Oyama*, S Shigeta, K Tsuji, H Tokunaga, M Shimada, N Yaegashi. *Tohoku University, Japan*

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Introduction Ovarian cancer is one of the most lethal gynecologic malignancies. Many patients are diagnosed in advanced stages of disease where the prognosis is poor due to the inevitable acquired resistance to platinum agents. Thus, novel therapeutic strategies effective for platinum-resistant cases are required. Zinc Finger Homeobox 4 (ZFHX4) has been known as one of the major transcription regulators in nerve and muscle differentiation. Recent researches including our genome-wide exploration indicate ZFHX4 is also involved in carcinogenesis and cancer progression. The objective of this study was to investigate the potential of ZFHX4 as a novel therapeutic target in ovarian cancer.

Methods Correlations between ZFHX4 mRNA expression and overall survival in 61 ovarian cancer cases treated at our institute and in the cases registered in TCGA database respectively were assessed by log-rank test. RNAi knockdown was introduced to several ovarian cancer cells to investigate the influence of ZFHX4 on cancer cell proliferation, migration and platinum sensitivity.

[Results] Both in our clinical dataset and TCGA data, the overall survival was significantly poor in the group in which ZFHX4 is highly expressed. In cell model assay, ZFHX4 knockdown significantly suppressed ovarian cancer cell proliferation. Decreased motility was observed in the cells treated with siRNA targeting ZFHX4 by scratch assay. Furthermore, ZFHX4 knockdown increased cisplatin sensitivity.

Conclusions Altogether, our results suggest ZFHX4 functions to promote cancer cell proliferation, migration and platinum-resistance. Interruption of ZFHX4 function independently or in combination with platinum agents has a potential to bring benefit for the treatment of ovarian cancer.

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221 PARAAORTIC LYMPHADENECTOMY IN CERVICAL CANCER STAGE IIIC1R INTERNATIONAL FEDERATION OF GYNECOLOGY AND OBSTETRICS 2018: EXPERIENCE AT THE INSTITUTO NACIONAL DE CANCEROLOGÍA

¹J Acosta*, ²J Rodriguez, ³J Velasquez, ⁴L Buitrago, ⁵O Forero, ⁶J Peralta, ¹J Saenz. ¹Department of Gynecology Oncology. Instituto Nacional de Cancerología, Colombia; ²Department of Gynecology Oncology. Instituto Nacional de Cancerología. Department of Gynecology and obstetrics. Section of Gynecology Oncology. Fundación Santa Fe de Bogotá, Colombia; ³Department of Clinical Oncology. Instituto Nacional de Cancerología, Colombia; ⁴Department of statistics. Universidad Nacional de Colombia. Department of Epidemiology. Universidad de la Sabana, Colombia; ⁵Department of Radiology. Instituto Nacional de Cancerología, Colombia; ⁶Department of Gynecology and Obstetrics. Universidad Nacional de Colombia, Colombia

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Introduction The objective of this study is to describe surgical and oncological outcomes of patients with cervical cancer stage IIIC1r FIGO 2018, underwent to staging paraaortic lymphadenectomy at the Instituto Nacional de Cancerología. Bogotá-Colombia, between January 2016 to March 2019.

Methods Retrospective study. Data collected included clinical characteristics, histopathological, surgical results. Furthermore, overall survival and disease-free survival were described in the population. A univariate descriptive analysis was performed. Survival curves were estimated with the Kaplan-Meier method. Statistical software R -Project version 3.6.2 was used.