713

PALBOCICLIB AND METFORMIN SHOW ANTICANCER EFFICACY IN HIGH GRADE SEROUS OVARIAN CANCER

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Palbociclib and metformin show anticancer efficacy in high grade serous ovarian cancer

Introduction/Background* Alterations in CDK-cyclin signaling pathway lead to cell cycle defects and induce continued cell proliferation, as well as genomic and chromosomal instability. Pharmacological inhibition of cyclin-dependent kinases 4 and

6 (CDK4/6) is a well-established anti-cancer treatment in breast cancer and is currently a subject of research in other tumors. Predictive biomarkers for response to CDK4/6 inhibitors include a functional retinoblastoma protein and cyclin D overexpression. According to the data from The Cancer Genome Atlas (TCGA), genomic aberrations that activate cyclin D, are observed in 20-30% of high grade serous ovarian cancer (HGSOC). Currently, there is a lack of data on CDK4/6 inhibition in ovarian cancer.

Metformin is a synthetic biguanide and is widely used as a first line antidiabetic drug. Besides that, anti-cancer efficacy of metformin due to downregulation of cyclin D in cancer cells was reported. Therefore, we hypothesize that metformin could be a potential partner for CDK4/6 inhibitors in cancer treatment and aim to investigate the anti-cancer efficacy of CDK4/

RESULTS:

Ovarian cancer 2D cell lines - Cellviability via MTT assay

Abstract 713 Figure 1

RESULTS:

Ovarian cancer 3D tumor spheroid model – Cellviability

Abstract 713 Figure 2

6 inhibitor palbociclib in combination with metformin in two-dimensional (2D) and three-dimensional (3D) HGSOC cultures. **Methodology** Four ovarian cancer cell lines were treated with palbociclib, or metformin, or combination of both agents. Cell viability was assessed using MTT assays and cell cycle arrest was detected using flow cytometry. Subsequently, the results were validated using 3D-tumor spheroid model.

Result(s)* A significant decrease in cell viability was detected in all four ovarian cancer cell lines under treatment with palbociclib (-99.5% in A2780; -97% in BIN67; -84% in OVCAR3; -61.4% in SKOV6), under treatment with metformin (-85.18%; -75.34%; -86.40%, -62.96%, respectively) and under treatment with the combination of both (-99.6%; -94.9%; -85.8%; -76.9%, respectively). Subsequently, the results were confirmed in 3D tumor spheroid model, where both agents showed synergetic anticancer efficacy. Both agents promoted cell cycle arrest in all four 2D cell lines.

Conclusion* Combination of CDK inhibitor palbociclib and metformin showed high anti-cancer efficacy in 5 ovarian cancer cell lines and in the three-dimensional tumor spheroid model. This effect is probably due to cyclin D-driven cell cycle arrest. Thus, cyclin/CDK pathway represents a novel therapeutic target in ovarian cancer.

718

INVESTIGATING IMPACT OF ULTRA-RADICAL SURGERY IN ADVANCED OVARIAN CANCER USING POPULATION LEVEL DATA LINKED TO THE SOCQER 2 MULTICENTRE STUDY

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Introduction/Background* The first population study investigating per protocol implementation of ultra-radical surgery (URS) as primary surgery reported that URS in advanced ovarian cancer (AOC) reduces the proportion treated surgically and does not improve survival.¹ We investigated this hypothesis using population level data for centers participating in the SOCQER 2 study

Abstract 718 Table 1 Proportion of treatment received in centres participating in the SOCQER2 study—population data analysis. Stage 3, 4 and stage unknown patients

	Proportion of treatment received in centres participating in the SOCQER2 study – population data analysis. Stage 3,4 and stage unknown patients.					
	Centres with >70% low SCS surgery (5/11 participating centres)		Centres with low SCS 35-50% and > 40% intermediate SCS surgery (3/11 participating centres).		Centres with >35% high SCS surgery (3/11 participating centres)	
Treatment within cancer network	N	%	n	%	n	%
No resection surgery/no chemotherapy	220	27.9	96	26.3	95	25.8
Chemotherapy only	217	27.5	55	15.1	83	22.6
Resection surgery only	42	5.3	25	6.8	49	13.3
Resection surgery and chemotherapy	309	39.2	189	51.8	141	38.3

Surgical treatment in the Socqer2 study	95% Confidence Interval			
	Median	Std. Error	Lower Bound	Upper Bound
Centres with >70% low SCS surgery	18.859	1.244	16.420	21.298
Centres with mainly low (35-50%) and > 40% intermediate SCS surgery	22.473	2.180	18.200	26.745
Centres with >35% high SCS surgery	24.017	1.810	20.469	27.565
Overall	20.929	1.009	18.950	22.907