AURANOFIN AS A POTENTIAL ANTICANCER DRUG IN EPITHELIAL OVARIAN CANCER

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Introduction/Background Ovarian Cancer (OC) is the most lethal gynecological disease. Surgery plus chemotherapy is the cornerstone of treatment. Eighty percent of patients who achieve full remission with first-line platinum-based therapy will develop a relapse due to OC platinum resistance. Auranofin (AF) has shown a significant antitumor activity both in vivo and in vitro studies in cancers, such as breast cancer. The primary objective is to evaluate AF effect on cellular pathways of primary epithelial OC cell cultures. Secondary object was to compare the response to AF versus cisplatin in ex-vivo primary OC cultures.

Methodology We analyzed primary ex-vivo OC cultures isolated by mechanical and enzymatic methods, obtained from 20 patients who had a primary cytoreduction for advanced OC between December 2020 and April 2021, versus three-dimensional spheroids from cell lines (A2780 and SKOV3). Cultures were treated with AF and cisplatin.

Results Subsequent treatment with increased AF concentrations on both primary ex vivo OC cultures and spheroids of the A2780 line showed that AF is able to inhibit both cellular cultures in a dose-dependent way. AF interferes with signaling pathways that play an important role in inflammation, chemoresistance and cell proliferation. Both in primary cultures and in spheroids AF reduces nuclear factor kappa-light-chain-enhancer of activated B cells (NF-kB) and phosphorylated protein kinase B (pAKT). Moreover, AF interferes on protein kinase C iota (PKCi) signaling in primary ex vivo cultures, while on the spheroids it decreases the expression of hypoxia inducible factor (HIF) and CA-125 levels. Finally, cultures of ex-vivo OC are more sensitive to AF than to cisplatin, with relative IC50 values of AF 3 to 9 times lower than those of cisplatin.

Conclusion Our results suggest that AF may represent a new option in OC therapy.

Conclusion Disease recurrence was more likely in patients with FIGO stage greater than 1a. However, one case of recurrence was noted in a patient with 1a disease. PCI score was higher in patients that later experienced recurrence, although not statistically significant. Future research should examine if PCI score can predict recurrence in larger patient populations.