promote 50% growth inhibition (IC50) for each cell line was calculated by sigmoidal regression using Origin 8.0 software. The Combination Reduction Index (CRI) was calculated as IC 50 of the metal complex + monoterpene / IC 50 of the metal complex alone. **Results:** Both silver complexes exhibited potent antiproliferative activity. The antiproliferative effect of silver complex I ranged from 4 μM to 10 μM in SCC and CM cell lines, whereas the antiproliferative effect of silver complex II ranged from 1 μM to 6 μM in the same cell lines. The association of silver complex I in combination with S-(-)-limonene resulted in synergism effect in the FaDu cell line with IC50 < 2 μM, CRI = 0.4. The association of silver complex II with both enantiomers demonstrated a partial synergistic effect in the FaDu and SK-MEL-28 cells, with IC50 <1.5 μM and CRI = 0.5. **Conclusion:** Silver complexes are promising candidates for in vivo studies as potential alternatives for the treatment of patients with SCC and CM. Additional experiments are necessary to evaluate their mechanism of action and toxicity. The study was supported by Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), Fundação de Apoio ao Ensino e à Pesquisa do Estado de São Paulo (FAPESP #2016/07729-4; #2023/09738-4 and Cancer Theranostics Innovation Center, (CancerThera), CEPID FAPESP #2021/10265-8).

Keywords: Combination, Limonene, Melanoma, Silver complexes, Squamous cell carcinoma.

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ROLE OF GENETIC VARIABILITY IN METABOLIC PATHWAYS ON CISPLATIN-INDUCED KIDNEY INJURY IN HEAD AND NECK CANCER PATIENTS

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A B S T R A C T

Introduction/Justification: Head and neck squamous cell carcinoma (HNSCC) is a prevalent malignancy responsible for approximately 5.0% of global cancer deaths. The standard treatment for locally advanced HNSCC involves cisplatin (CDDP)-based chemotherapy and radiotherapy, which can lead to significant adverse effects, particularly nephrotoxicity. It is already well known that the efficacy of CDDP as well as its side effects vary in distinct patients with HNSCC, and single nucleotide variants (SNVs) in genes that act in CDDP metabolism constitute a plausible explanation for this finding. **Objectives:** To investigate the roles of SNVs GSTM1, GSTT1, GSTP1 c.313A>G, XPC c.2815A>C, XPD c.934G>A and c.2251A>C, XPF c.2505T>C, ERCC1 c.354C>T, MLH1 c.93G>A, MSH2 c.211+9C>G, MSH3 c.3133A>G, EXO1 c.1765G>A, TP53 c.215G>C, CASP3 c.-1191A>G and c.-182-247G>T, FAS c.-1378G>A and c.-671A>G, and FASL c.-844C>T SNVs on kidney function outcomes in HNSCC patients undergoing CDDP treatment. **Materials and Methods:** A total of 109 patients with locally advanced HNSCC treated with CDDP were included in the study. Genotypes were determined using polymerase chain reaction (PCR). Renal function was assessed by calculating estimating glomerular filtration rate (eGFR) using the 2021 Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation, before treatment initiation and 30 days post-treatment. The percentage variation in kidney function was calculated by determining the difference between baseline (pre-chemotherapy) and follow-up (post-chemotherapy) values for eGFR divided by the pre-chemotherapy value and represented as ΔeGFR. **Results:** Patients with the GSTT1 present and ERCC1 c.354CT or TT isolated genotypes presented a decline in kidney function of 4.94% and 8.94%, respectively. A decline of 17.67% in renal function post-CDDP treatment was observed in patients with the GSTT1 present combined with TP53 c.215CC genotype. Patients with the GSTP1 c.313AG or GG and ERCC1 c.354CT or TTC>T (17.57%), MLH1 c.93GA or A (12.49%), or MSH3 c.3133AG or GG (12.19%) combined genotypes showed a reduction in renal function after CDDP treatment. Renal function declines of 18.85% and 13.38% were observed in patients with ERCC1 c.354CT or TT and MLH1 c.93GA or AA or MSH3 c.3133AG or GG combined genotypes, respectively. **Conclusion:** Our data indicates, for the first time, preliminary evidence that combined inherited abnormalities, SNVs that act in CDDP metabolism, act as independent factors for nephrotoxicity in HNSCC patients and can be used to select patients for personalized treatments that promote renal protection and reduced nephrotoxicity. **Acknowledgements:** The study was supported by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) (grant number 88887.513947/2020-00), the Postdoctoral Program (PPPD) at the University of Campinas (UNICAMP) (Postdoctoral ID number: 326285), and the Fundação de Apoio ao Ensino e à Pesquisa do Estado de São Paulo (FAPESP) Cancer Theranostics Innovation Center (CancerThera) (FAPESP 2021/10265-8).

Keywords: Cisplatin, Head and neck squamous cell carcinoma, Nephrotoxicity, Single nucleotide variants.

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KIF13B C.*3163G>A SINGLE NUCLEOTIDE VARIANT ON OROPHARYNGEAL SQUAMOUS CELL CARCINOMA SUSCEPTIBILITY AND TUMOR CHARACTERISTICS

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