Ondansetron Co-Treatment Increases Risk of Cisplatin Nephrotoxicity. LE Thompson, (PhD, SSPPS), X Wen, J Jorgensen, JN Palan, CL Doherty, BT Buckley, EA Jaimes, LM Aleksunes, MS Joy, Skaggs School of Pharmacy and Pharmaceutical Sciences, University of Colorado Anschutz Medical Campus, Aurora, CO.

Cisplatin (CIS), a common chemotherapeutic, causes acute kidney injury (AKI) in up to one-third of patients. Previous reports have indicated that maximum plasma concentration (Cmax) or area under the plasma concentration vs time curve (AUC) of platinum (Pt) increase risk of AKI. Ondansetron, a commonly co-prescribed 5-HT_3 antagonist antiemetic drug in patients receiving CIS, has been associated with enhanced risk of AKI in rodents and retrospective clinical studies.

As part of study NCT03817970, patients (n=23) undergoing their first or second round of CIS chemotherapy (≥25 mg/m^2) were prospectively randomized to one of three antiemetic drugs (ondansetron 8 mg p.o., granisetron 2 mg p.o., or palonosetron 0.25 mg i.v.). Total Pt plasma concentrations were quantified using inductively coupled plasma-mass-spectrometry (ICP/MS). Pharmacokinetic analyses were performed using Certara Phoenix™.

Patients who received ondansetron had significantly increased total Pt plasma Cmax levels (normalized by CIS dose) compared to patients receiving granisetron or palonosetron ($p<0.01$). Ondansetron-treated patients also had the highest AUC from 0-2 hours (normalized by CIS dose) ($p=0.02$). Moreover, ondansetron-treated patients had the largest average decrease in estimated glomerular filtration rate (eGFR) ($p=0.22$) and demonstrated a significantly larger increase in urinary kidney injury molecule-1 (KIM-1) following CIS treatment ($p=0.03$) compared to granisetron and palonosetron-treated patients

CIS-treated cancer patients prescribed ondansetron exhibited decreased kidney function when compared to patients receiving granisetron or palonosetron.