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Nanoparticle entrapped docetaxel (CPC634) enhances intratumoral docetaxel exposure compared to conventional docetaxel (Cd) in patients with solid tumors.

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Background: Failure or resistance to chemotherapy may be caused by sub-therapeutic intratumoral drug levels. Nanomedicine aim to improve intratumoral drug exposure. CPC634 is a nanoparticle entrapping docetaxel. We hypothesized that CPC634 increases intratumoral docetaxel exposure. **Methods:** In this randomized cross-over study we assessed intratumoral and plasma pharmacokinetics (PK) of docetaxel after intravenous administration of CPC634 and conventional docetaxel (Cd). The study was powered to identify an 25% increase in intratumoral docetaxel exposure of CPC634 relative to Cd. Patients (≥18 years) were randomized to receive 75 mg/m_2 CPC634 in cycle 1 and Cd in cycle 2 or *vice versa*. After drug administration, patients underwent tumor biopsies during both cycles. Total docetaxel was determined for both drugs and released docetaxel for *CPC634* in tumor tissue and in plasma with a validated LC-MS/MS method. PK data were analyzed with mixed model analysis. **Results:** Sixteen evaluable patients were included. Intratumoral PK revealed a 323% (95% CI: 148,621) higher total docetaxel ($p < 0.001$) for CPC634. Released docetaxel for CPC634 was comparable to total docetaxel levels for Cd (95% CI: -35-,67) ($p = 0.43$). Plasma released docetaxel for CPC634 exhibited an 89% (95% CI: 86, 91) lower ($p < 0.001$) peak plasma concentration (C_{max}) and 81% (95% CI: 46, 125) higher ($p < 0.001$) area under the curve (AUC) relative to Cd. **Conclusions:** CPC634 resulted in higher intratumoral total docetaxel and comparable released docetaxel levels relative to total docetaxel for Cd. CPC634 had a favorable plasma PK profile with a lower C_{max} and prolonged higher systemic exposure relative to Cd. These results indicate that CPC634 could improve intratumoral docetaxel exposure compared to Cd. Additional studies assessing the intratumoral exposure to CPC634 (NCT0371243) and a phase II efficacy study of CPC634 in patients with platinum resistant ovarian cancer (NCT03742713) are currently ongoing.