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First-in-human imaging of nanoparticle entrapped docetaxel (CPC634) in patients with advanced solid tumors using ^{89}Zr-Df-CPC634 PET/CT.

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Background: CPC634 is a nanoparticle entrapping docetaxel designed to improve tumor accumulation and tolerability compared to conventionally administered docetaxel by taking advantage of the presumed enhanced permeability and retention (EPR) effect. In vivo imaging with zirconium-89 (^{89}Zr)-desferal (Df)-CPC634 will provide valuable information on its biodistribution and will quantify tumor retention. **Methods**: Patients with solid tumors not amenable to standard therapy received 37 MBq, 0.1-2mg of ^{89}Zr-Df-CPC634 tracer and whole body PET/CT scans were obtained at 2, 24 and 96h post-injection (p.i.). Patients were administered CPC634 (60mg/m$_2$) two weeks later followed by a second tracer injection and scans at 24 and 96h p.i. Biodistribution was quantified by delineating organs of interest and calculating mean %ID/kg. Visual tumor retention was defined as focal uptake in tumor lesions exceeding local background and quantified as standardized uptake peak values (SUV_{peak}) in volumes of interest. **Results**: Five patients were included. Biodistribution of ^{89}Zr-Df-CPC634 showed significant retention in healthy liver, and spleen compared to lung (respectively 2.54, 1.61 and 0.56 mean %ID/kg at 96h p.i.), supporting apparent opsonization of nanoparticles in cells of the reticuloendothelial system. Visual retention was observed in 16/37 evaluable tumor lesions with the highest intensity at 96h p.i, compatible with the assumed EPR effect. Tumor retention showed intra- and interpatient heterogeneity, with a mean %ID/kg of 3.43 [1.14-9.32]. Pre-administering unlabeled CPC634 did not change the mean tumor retention of ^{89}Zr-Df-CPC634 (at 96h p.i. mean 3.50 %ID/kg [1.64-9.97]), however, four additional lesions were visible in comparison to tracer only. **Conclusions**: The biodistribution of ^{89}Zr-Df-CPC634 was consistent with a prolonged exposure of nanoparticle containing docetaxel. ^{89}Zr-Df-CPC634 showed high retention in tumors confirming the EPR effect of these nanoparticle in humans, and supporting their further development for tumor targeting of therapeutic agents. A Phase II efficacy study in platinum resistant ovarian cancer (NTC03742713) is currently ongoing.