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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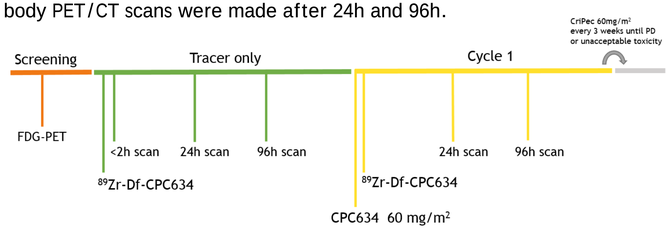
BACKGROUND

CPC634 is a novel nanoparticle entrapping docetaxel

- It is designed to improve tumor accumulation and tolerability compared to conventional docetaxel.
- Non-invasive imaging with PET/CT was realized by labelling this nanoparticle with zirconium-89 (^{89}Zr) using a desferal (Df) linker on the nanoparticle surface.

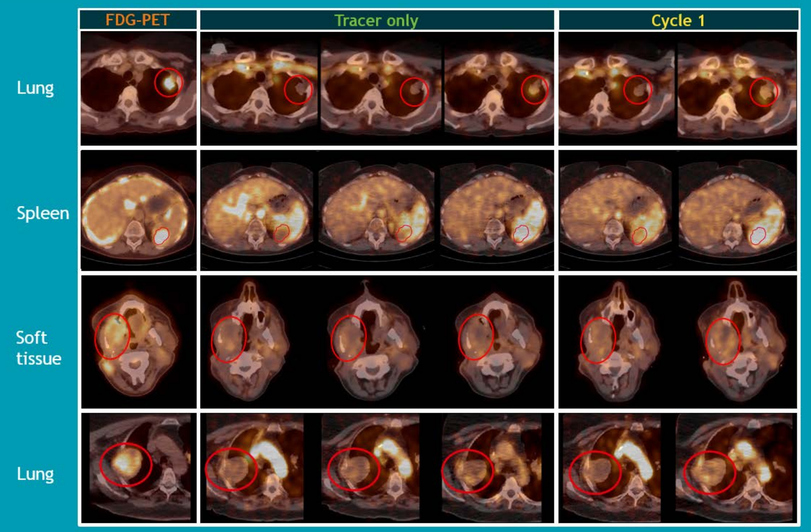
METHODS

- Patients with solid tumors were injected with 37 MBq ^{89}Zr-Df-CPC634, and whole body PET/CT scans were obtained at <2h, 72h and 144h post injection (p.i.) (referred to as '*tracer only*').
- Two weeks thereafter they received their second ^{89}Zr-Df-CPC634, within 2 hours after administering the first cycle of CPC634 60 mg/m^2 ('*cycle 1*').
- Whole body PET/CT scans were made after 24h and 96h.



The accumulation of nanoparticle-entrapped docetaxel can be visualized and quantified in tumors using PET/CT imaging, providing evidence for the enhanced permeability and retention effect in humans.

Figure 1



RESULTS

- Biodistribution of ^{89}Zr-Df-CPC634 reveals longevity in the bloodstream, and accumulation in healthy liver and spleen. There were no significant differences between *tracer only* vs. *cycle 1* regarding biodistribution. Figure 2
- 16/46 (35%) evaluable tumors showed accumulation of ^{89}Zr-Df-CPC634. Different patterns of accumulation were observed. Figure 1 and Table 1
- ^{89}Zr-Df-CPC634 accumulated in tumor lesions over time. The highest %ID/kg was found at 96 hours p.i. with a median of 2.93 (range 1.14 – 9.97). Figure 3
- Comparison of *tracer only* and *cycle 1* did not reveal quantitative differences in tumor accumulation. However, in *cycle 1* more lesions were visually positive (at 96h p.i. 16 for cycle 1 vs. 12 for tracer only). Figure 3

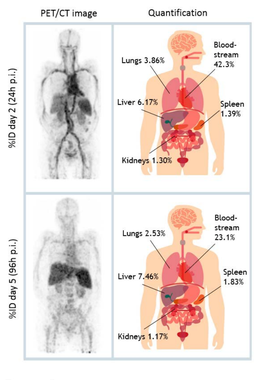
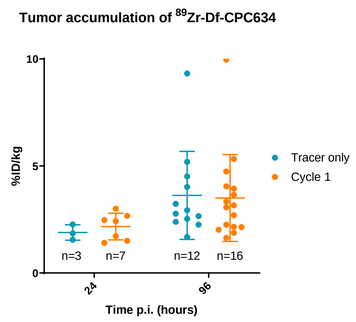


Figure 2

Table 1

Study subject	Location	N	Lesions >20mm	FDG uptake	^{89}Zr accumulation at any time AND >20mm	^{89}Zr uptake pattern N
1 Ovarian ca	Spleen	3	2 (67%)	3 (100%)	1 (50%)	Homogenous: 1
2 Esophageal ca	Liver Soft tissue Bone	10 1 1	10 (100%) 1 (100%) 0	10 (100%) 1 (100%) 1 (100%)	0 0 0	
3 Endometrial ca	Lung	2	2 (100%)	2 (100%)	2 (100%)	Spotted: 2
4 Colorectal ca	Lung Liver Soft tissue	30 7 7	10 (33%) 3 (43%) 0	27 (90%) 7 (100%) 6 (86%)	6 (60%) 0 0	Spotted: 3 Rim: 3
5 Myo-epithelial ca	Soft tissue Subcutaneous Lung Bone	24 6 6 3	14 (58%) 2 (33%) 1 (17%) 1 (33%)	22 (92%) 5 (83%) 3 (50%) 3 (100%)	5 (36%) 1 (50%) 1 (100%) 0	Spotted: 3 Center: 2 Spotted: 1 Spotted: 1
Total		100	46 (46%)	90 (90%)	16/46 (35%)	Homogenous: 1 Spotted: 10 Center: 2 Rim: 3

Figure 3



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