Supporting Information

to

Tumor microenvironment in focus: LA-ICP-MS bioimaging of a preclinical tumor model upon treatment with platinum(IV)-based anticancer drugs

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Table S1. Administration regimens for satraplatin, compound **1**, **2**, **3** and oxaliplatin and platinum concentrations in tumor and kidney of CT-26 bearing mice (n=4) after treatment with the respective compounds.

compound	**form of admin.**	**admin. dose [mg/kg]**	**Pt admin.* [mg/kg]**	**Pt accumulation in µg/g**	
				tumor (n=4)**	**kidney** (n=4)**
satraplatin	p.o.	40.0	15.63	0.55 ± 0.18	2.53 ± 0.39
1	p.o.	51.7	15.63	2.26 ± 1.38	7.23 ± 1.11
1	i.p.	8.5	2.58	1.85 ± 0.69	9.02 ± 1.10
2	i.p.	10.0	2.58	0.74 ± 0.17	2.18 ± 0.33
3	i.p.	30.0	11.04	4.96 ± 0.89	10.49 ± 1.73
oxaliplatin	i.v.	9.0	4.42	0.98 ± 0.34	4.54 ± 0.72

* calculated from applied dose

** values taken from ref.[29] for satraplatin, compound **1** and **2**; and from ref.[30] for oxaliplatin and compound **3**

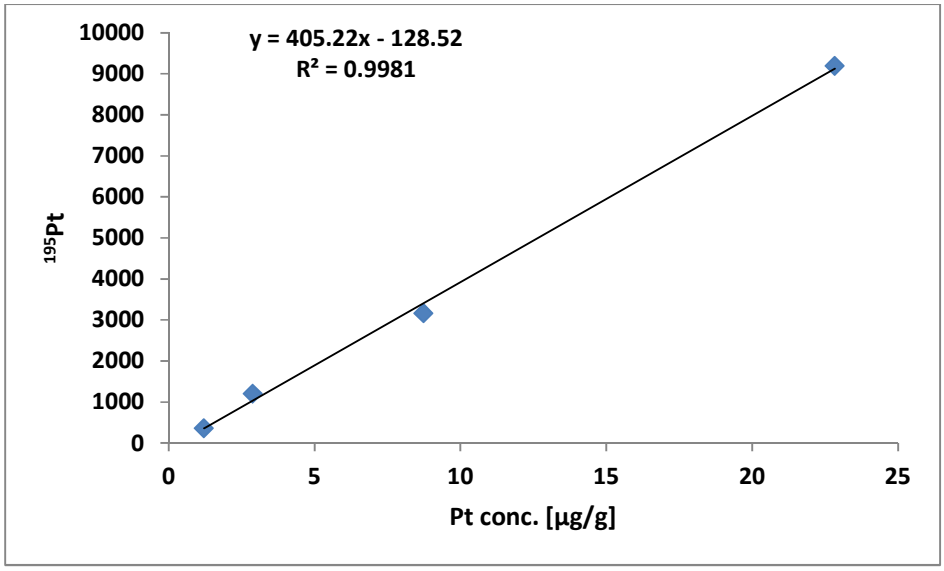

Figure S1. Representative calibration curve (valid for tumor upon treatment with compound **2**, 10 mg/kg, i.p.) for the quantification of platinum in tumor and kidney sections by LA-ICP-MS. Counts per second (CPS) of the registered isotope ^{195}Pt are plotted against the experimentally determined platinum concentrations by ICP-MS in the matrix-matched standards.

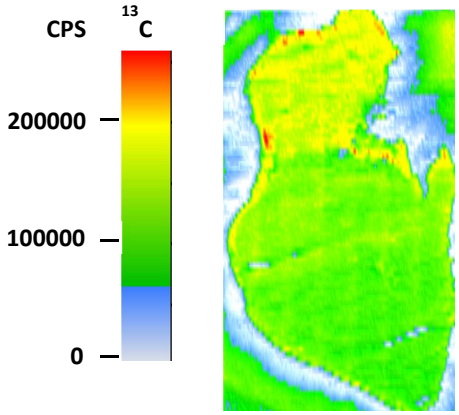

Figure S2. ^{13}C distribution as indication of organic matter in an ablated tumor section upon treatment with compound 1 (51.7 mg/kg, p.o.). Organic matter outside the tumor originates from the embedding medium.

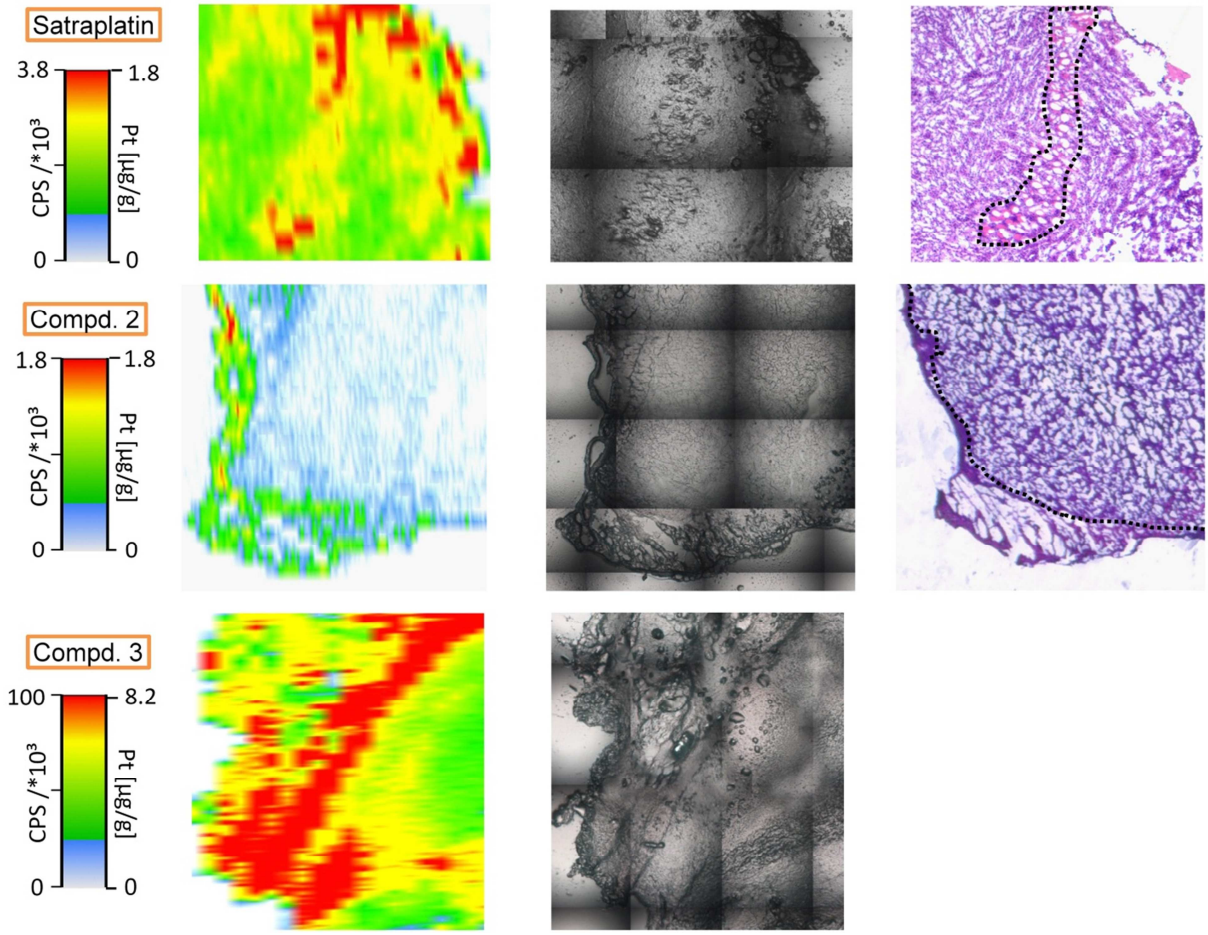

Figure S3. Detailed view of ablated tumor samples after treatment with satraplatin (p.o., top), compound **2** (i.p., middle) or compound **3** (i.p., bottom); laser platinum image (left), sample map taken prior to laser ablation (middle) and H&E-stained cryosection (right). The dotted spots in the H&E-stained slides correspond to loose connective tissue.

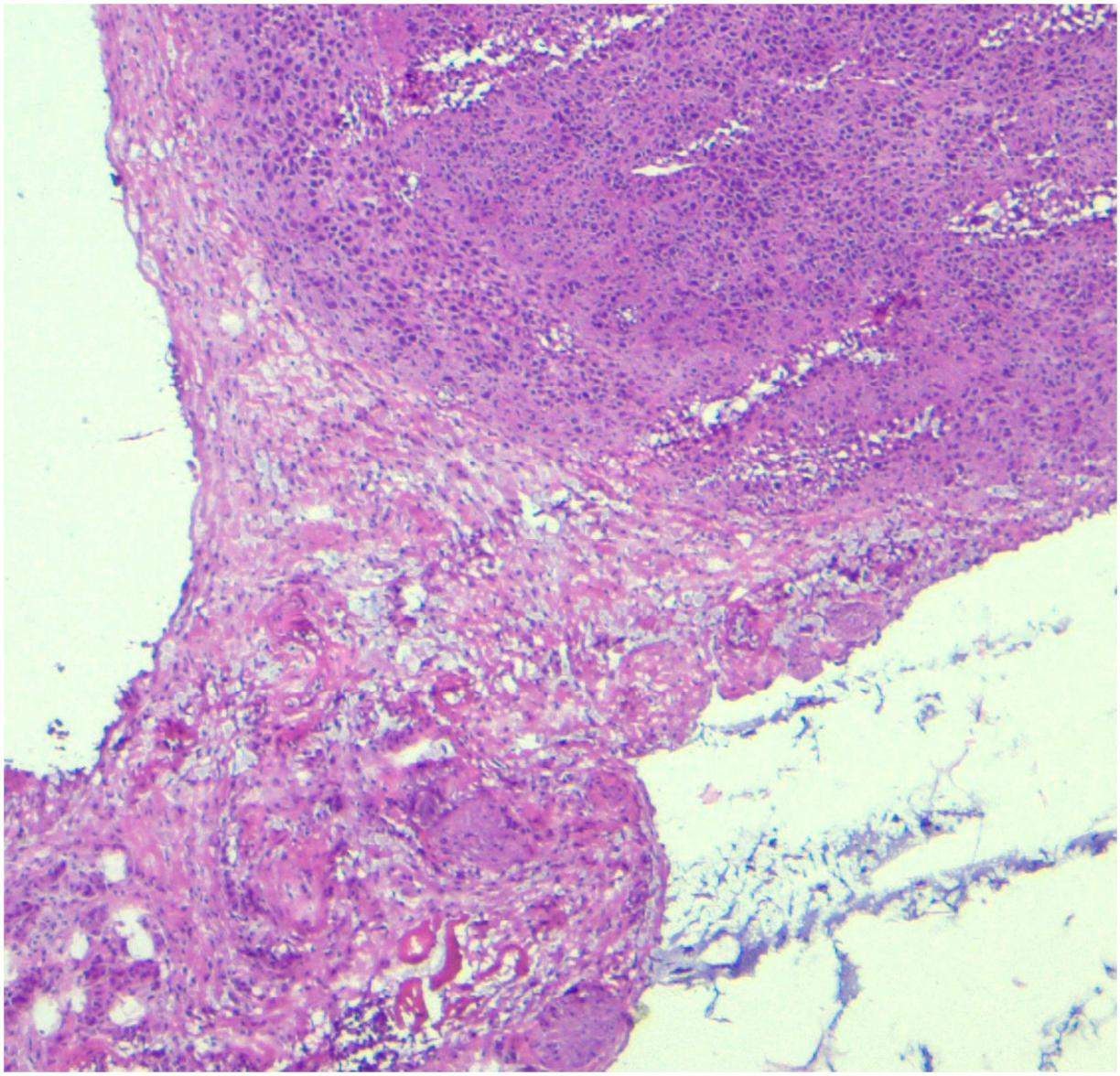

Figure S4. HE stained, enlarged image of the tumor treated with oxaliplatin (i.v.), corresponding to Figure 3, bottom. Loose connective tissue with sparsely scattered tumor cells (lower part) and areas of necrotic tissue as well as tumor nodules composed of mitotically active, highly atypical cells (upper part) are displayed.

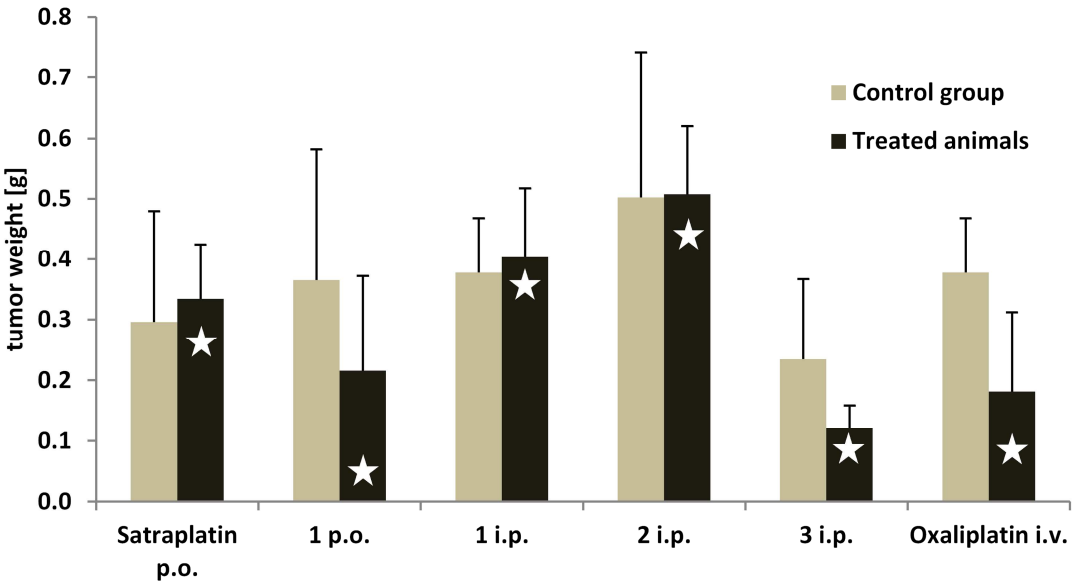

Figure S5. Anticancer activity of the test compounds. CT-26 cells were injected subcutaneously into the right flank of BALB/c mice. Mice were treated on day 4, 7, 11, and 14 with the indicated compounds. Animals were sacrificed on day 15 and tumors were collected. The white stars indicate the tumor weight of the single mouse subjected to LA-ICP-MS analysis after treatment with the respective compound.

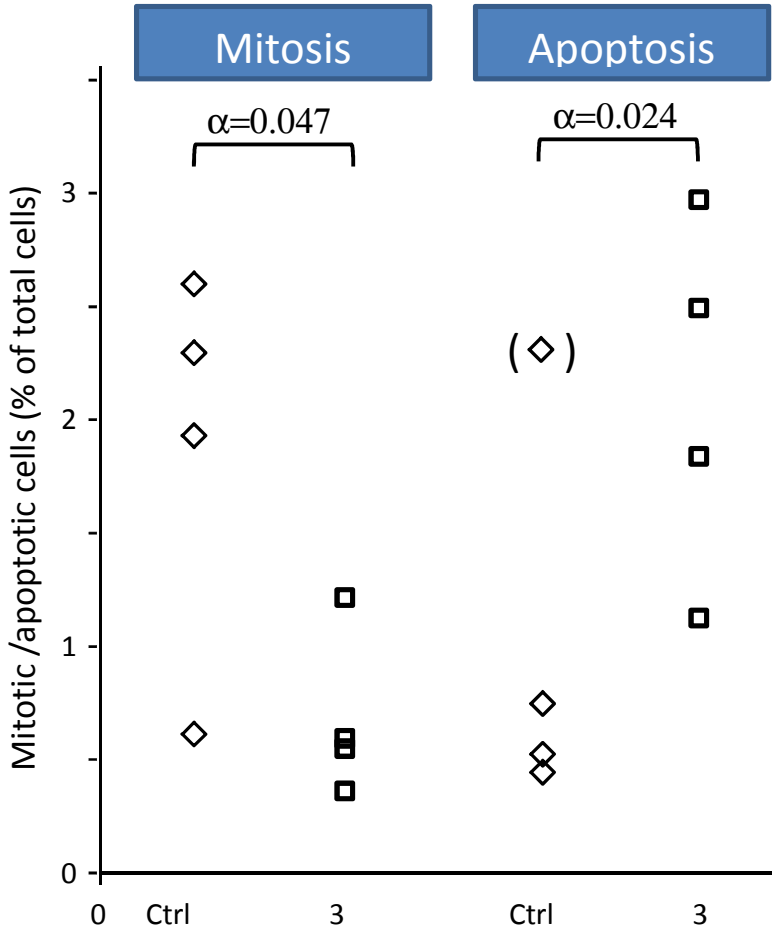

Figure S6. Fraction of mitotic and apoptotic cells in control animals (n=4, ◊) and animals treated with compound 3 (n=4, □). (◊) indicates an outlier. Rates of mitosis and apoptosis differed significantly from control animals ($\alpha<0.05$ based on ANOVA analysis).

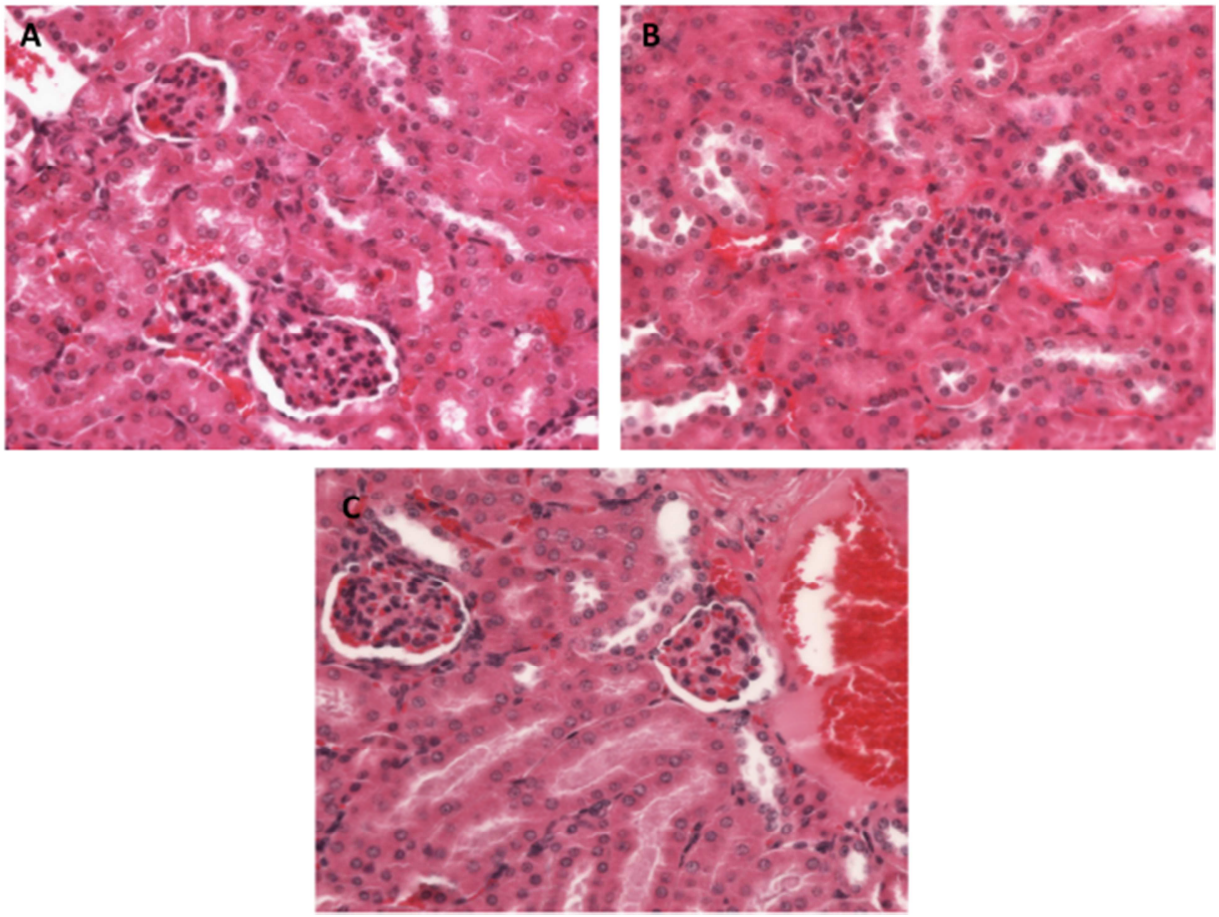

Figure S7. H&E-stained mouse kidney sections, cortex (40x). (A) control mouse (B) oxaliplatin (C) satraplatin.