46 Gy (43–48). When radiation, drugs and heat were combined the TCD50 was 35 Gy (32−38), regardless of whether the drugs were CA4DP or CA4DP+HDZ.
Conclusions: CA4DP significantly increased Hct and MABP. This MABP increase, but not Hct, could be reversed with the antihypertensive drug HDZ. CA4DP also significantly improved tumour response to radiation or thermoradiation, neither of which was influenced by the addition of HDZ.

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Comparison of the effect of patupilone (EPO906) and other cytotoxic drugs on interstitial fluid pressure (IFP) and growth of human ovarian (1A9 and 1A9PTX10) and lung (A549 and A549.B40) xenografts in athymic mice

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Patupilone (PAT) is a natural, non-taxane microtubule stabilizing agent. PAT binds beta-tubulin with a higher affinity than taxanes and potently inhibits growth of a broad range of human tumor cell lines *in vitro* and *in vivo*, including multi-drug resistant cells over-expressing the P-gp drug efflux pump. In this study, we compared the efficacy of PAT with the drugs paclitaxel (PTX), docetaxel (DOC) and pegylated liposomal doxorubicin (Doxil) on human tumor xenografts with β-tubulin mutations: ovarian xenografts 1A9 (PTX-sensitive) and 1A9PTX10 (PTX-resistant) and on NSCLC xenografts A549 (PAT-sensitive) and A549.B40 (PAT-resistant). We also measured their effects on the IFP of 1A9 and 1A9PTX10 tumors. Xenograft tumors were grown ectopically in nude mice. Efficacy (TVol) and IFP (mm Hg) were measured in reference to vehicle-treated controls to give a T/C_{TVol} and T/C_{IFP} respectively. IFP was measured by insertion of a needle (WIN method). Data are summarised as mean T/C (ratio of treated divided by vehicle-control) with significance set at $p < 0.05$.
PAT treatment (2−4 mg/kg qw iv) dose-dependently inhibited 1A9 (max T/C_{TVol}=0.01) and 1A9PTX10 (max T/C_{TVol}=0.22) tumor growth and significantly decreased the IFP (max T/C_{IFP} = 0.04 and 0.15 for 1A9 and 1A9PTX10 respectively). Doxil (12 mg/kg qw iv) affected significantly the growth of 1A9 and 1A9PTX10 tumors (max T/C_{TVol}=0.06 and 0.13 respectively) and IFP of 1A9PTX10 tumor (max T/C_{IFP} = 0.21). PTX treatment (15−20 mg/kg iv q3w) abrogated 1A9 tumor growth (max T/C_{TVol}=0.05), and significantly decreased the tumor IFP of 1A9PTX10 tumors (max T/C_{IFP} = 0.42) but had no effect on their growth (max T/C_{TVol}=0.96).
PAT Treatment (2−4 mg/kg qw iv) dose-dependently inhibited A549 tumor growth (max T/C_{TVol} = −0.05) and had a weak effect on A549.B40 tumors (max T/C_{TVol}=0.61). Similarly, PTX and DOC (25 mg/kg qw iv) induced regression of A549 tumors (max T/C_{TVol} = −0.23 and −0.27 respectively) but had no significant effect on A549.B40 tumors (max T/C_{TVol}=0.73 and 0.65 respectively).
These data confirm that PAT retains activity against PTX-resistant ovarian tumors; while showing similar activity to Doxil. Interestingly, PAT showed similar activity to PTX and DOC in tumors selected for PAT-resistance. The PTX-driven decrease in IFP of PTX-resistant tumors suggests that IFP, and by inference tumor blood volume (Ferretti et al, Clin Cancer Res, 2005), is not causally related to efficacy, but is a biomarker of tumor drug exposure.