Summary

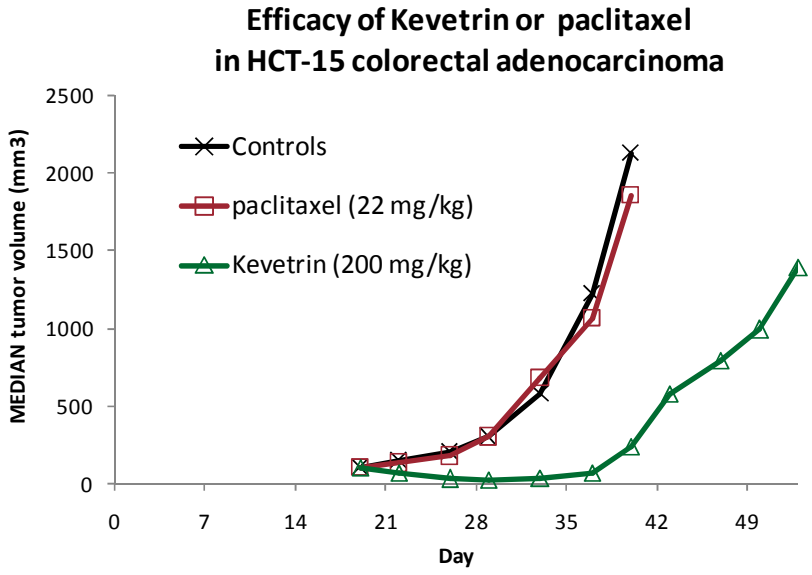
Kevetrin is effective in a mouse model of human colorectal adenocarcinoma: HCT-15

- Kevetrin (200 mg/kg IP x 3 doses)
  - 43% tumor growth delay compared to controls
  - 43% tumor growth delay compared to paclitaxel (22 mg/kg IV x 4 doses)

Details

HCT-15 is a human colorectal adenocarcinoma that has a mutated p53 tumor suppressor gene and overexpresses P-glycoprotein. P-glycoprotein acts as an efflux pump resulting in decreased intracellular accumulation of certain drugs contributing to drug resistance. Nude mice were implanted with HCT-15 subcutaneously in the right flank. Once tumors reached, on average, ~100 mm^3, the mice were grouped according to similar tumor size ranges. Mice were treated intraperitoneally with 200 mg/kg Kevetrin every other day for 3 doses. For comparison, another group of mice were treated with 22 mg/kg paclitaxel IV every other day for 4 doses. Another group of mice remained untreated to serve as controls. Tumors were measured three times per week.

The results of the experiment, presented as median tumor volumes over time, are shown below:



The growth of HCT-15 human colorectal adenocarcinoma was significantly delayed ($p<0.06$) following treatment with Kevetrin 43% compared to controls, whereas paclitaxel had no efficacy in these tumors producing 0% tumor growth delay, respectively, compared to controls. Tumor growth delay with Kevetrin was also significantly greater compared with paclitaxel ($p<0.06$). On measurements of tumor volume at day 40, Kevetrin was significantly more effective than controls or paclitaxel ($p<0.01$).

These results demonstrated that Kevetrin, but not paclitaxel, had potent anti-tumor activity against a human colorectal adenocarcinoma xenograft tumor model, HCT-15. This study supports the development of Kevetrin in colorectal adenocarcinoma indications, particularly in cases where tumors have become resistant to standard chemotherapy.