Summary

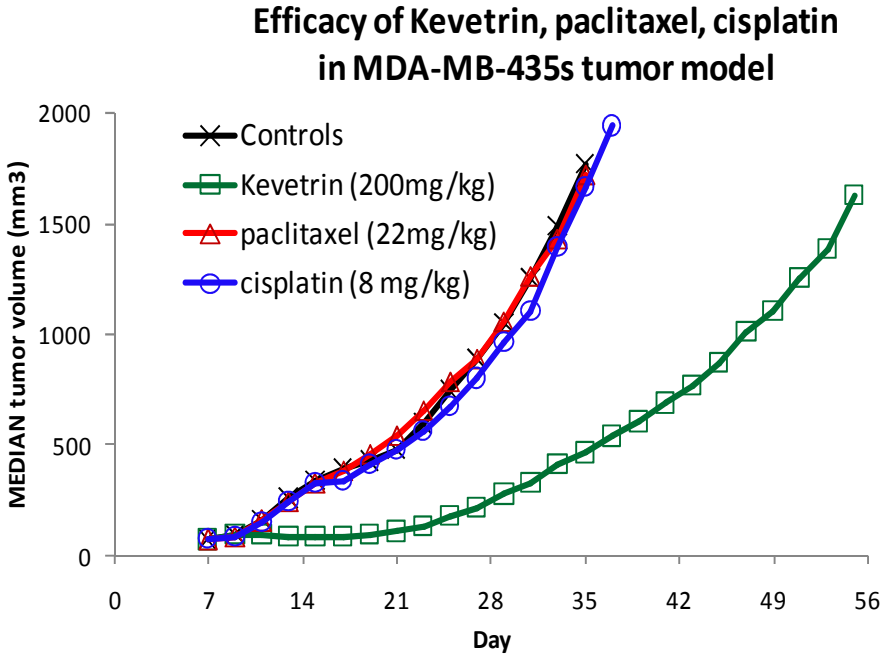
Kevetrin is effective in mouse models of human breast cancer: **MDA-MB-435S**

- Kevetrin (200 mg/kg IP x 3 doses)
  - 62% to 68% tumor growth delay compared to controls
  - 62% to 79% tumor growth delay compared to paclitaxel (22 mg/kg IV x 4 doses)
  - 52% tumor growth delay compared to cisplatin (8mg/kg IP x 1 dose)

Details

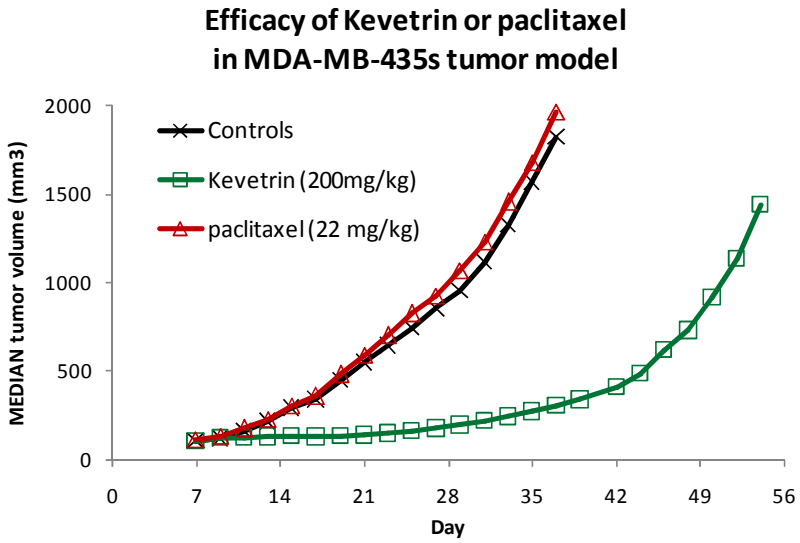
Nude mice were implanted with MDA-MB-435S, a human breast carcinoma cell line, subcutaneously in the right flank. Once tumors reached, on average, ~90 mm^3, the mice were grouped according to similar tumor size ranges. Mice were treated intraperitoneally with 200 mg/kg Kevetrin every other day for 3 doses. For comparison, another group of mice were treated with 22 mg/kg paclitaxel IV every other day for 4 doses or a single dose of 8 mg/kg cisplatin IP. Another group of mice remained untreated to serve as controls. Tumors were measured three times per week.

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



The growth of MDA-MB-435S human breast carcinoma tumors was significantly delayed ($p<0.01$) following treatment with Kevetrin 62% compared to controls, whereas neither paclitaxel nor cisplatin had efficacy in these tumors producing 0% or 7% tumor growth delay, respectively, compared to controls. Tumor growth delay with Kevetrin was also significantly greater compared with paclitaxel or cisplatin ($p<0.01$). On measurements of tumor volume at day 35, Kevetrin was significantly more effective than controls, paclitaxel, or cisplatin ($p<0.01$).

The results of the repeat experiment, in which cisplatin was not included, are shown below:



In this experiment, the growth of MDA-MB-435S human breast carcinoma tumors was significantly delayed ($p<0.01$) following treatment with Kevetrin 68% compared to controls, whereas paclitaxel had no efficacy in these tumors producing -6% tumor growth delay compared to controls. Tumor growth delay with Kevetrin was also significantly greater than with paclitaxel ($p<0.01$). On measurements of tumor volume at day 37, 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 breast carcinoma xenograft tumor model, MDA-MB-435S, a taxane resistant, estrogen receptor-negative, human breast carcinoma cell line. These studies support the development of Kevetrin in breast carcinoma indications, particularly in cases where tumors have become resistant to standard chemotherapy.