Summary

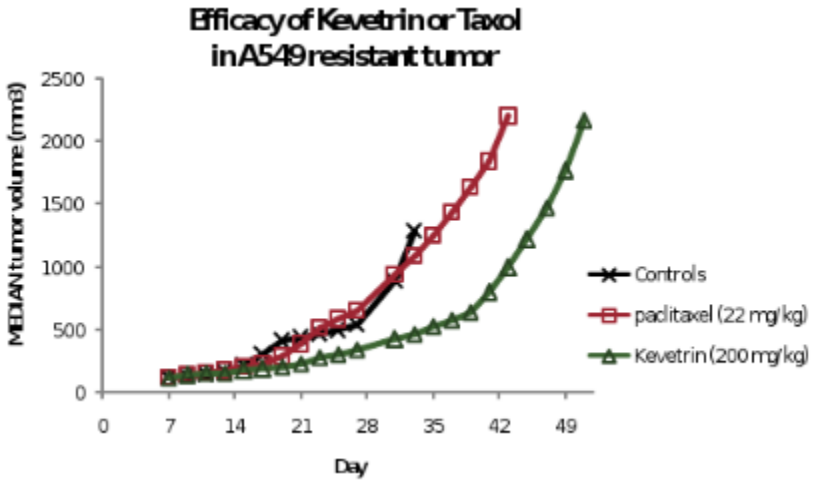
Kevetrin is effective in mouse models of human lung cancer : **A549**

- Kevetrin (200 mg/kg IVIP x 3 doses)
  - 33% to 111% tumor growth delay compared to controls
  - 33% to 100% tumor growth delay compared to paclitaxel (22 mg/kg IV x 4 doses)
- Only 3% to 4% decrease in animal weight

Details

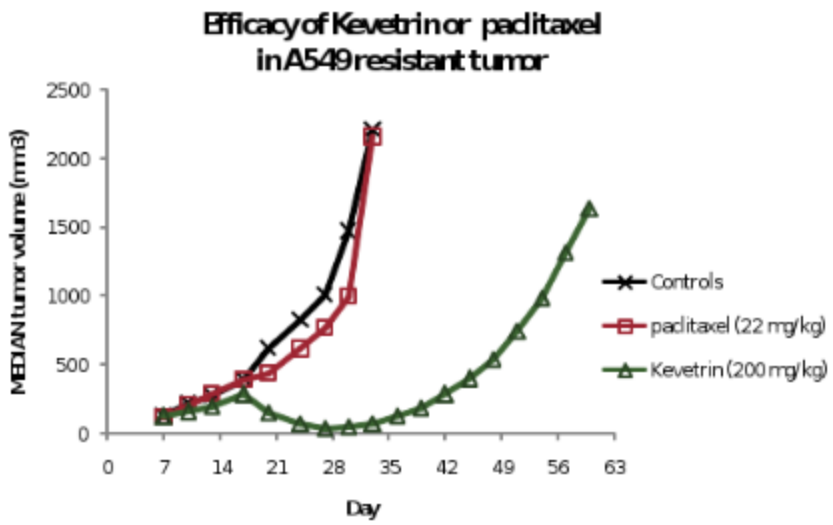
Kevetrin was shown to be effective in mouse models of human lung cancer. Nude mice were implanted with A-549, a multi-drug resistant human lung non small cell lung carcinoma (NSCLC) cell line, subcutaneously the right flank. Once tumors reached, on average, ~120 mm^3, the mice were grouped according to similar tumor size ranges. Mice were treated intravenously 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. During treatments, mice were observed daily for any adverse affects and mouse body weights were measured.

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



The growth of A549 human lung adenocarcinoma tumors was significantly delayed ($p < 0.01$) following treatment with Kevetrin to 33%, whereas paclitaxel had little efficacy in these tumors producing a no tumor growth delay.

The results of the repeat experiment are shown below:



In this experiment, the growth of A549 human lung adenocarcinoma tumors was significantly delayed ($p < 0.01$) following treatment with Kevetrin to 111%, whereas paclitaxel had little efficacy in these tumors producing a tumor growth delay of only 11%. A significant therapeutic index was achieved since during treatment, Kevetrin resulted in only a 3% to 4%, but transient, decrease in average animal weight.

These results demonstrated that Kevetrin, but not paclitaxel, had potent anti-tumor activity against a human lung adenocarcinoma xenograft tumor model, A549, at a dose and schedule that was well-tolerated as indicated by a small transient weight loss during treatment. These studies support the development of Kevetrin in lung carcinoma indications, particularly in cases where tumors have become resistant to standard chemotherapy.