

Summary

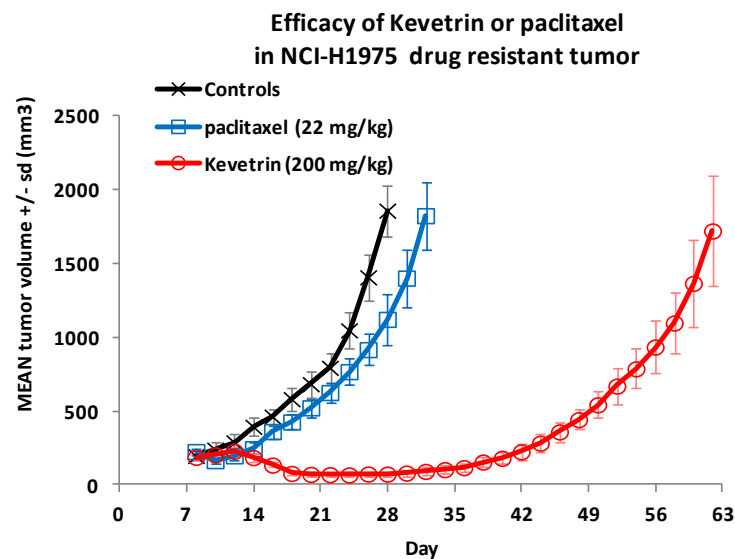
Kevetrin is effective in mouse models of human lung cancer : **NCI-H1975**

- Kevetrin (200 mg/kg IP x 3 doses)
 - 142% to 156% tumor growth delay compared to controls
 - 44% to 107% tumor growth delay compared to paclitaxel (22 mg/kg IV x 4 doses)
- No decrease in animal weight

Details

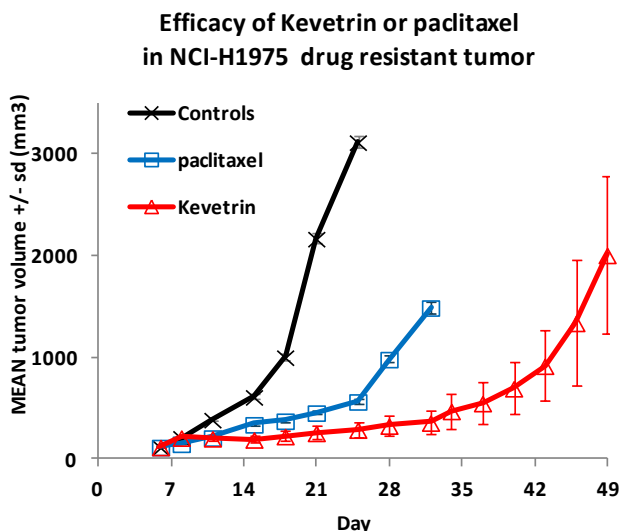
Nude mice were implanted with NCI-H1975, a multi-drug resistant human lung non small cell lung carcinoma (NSCLC) cell line, subcutaneously in the right flank. Once tumors reached, on average, ~120 to 200 mm³, the mice were grouped according to similar tumor size ranges. Mice were treated intraperitoneally 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. During treatments, mice were observed daily for any adverse affects and mouse body weights were measured.

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



The growth of NCI-H1975 human lung adenocarcinoma tumors was significantly delayed ($p<0.01$) following treatment with Kevetrin 142% compared to controls, whereas paclitaxel had little efficacy in these tumors producing a tumor growth delay of only 17% 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 28, Kevetrin was significantly more effective than controls or paclitaxel ($p<0.01$).

The results of the repeat experiment are shown below:



In this experiment, the growth of NCI-H1975 human lung adenocarcinoma tumors was significantly delayed ($p<0.01$) following treatment with Kevetrin 156% compared to controls, whereas paclitaxel had only moderate efficacy in these tumors producing a tumor growth delay of 78% 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 25, Kevetrin was significantly more effective than controls or paclitaxel ($p<0.01$). A significant therapeutic index was achieved since no weight loss occurred during treatment with Kevetrin.

These results demonstrated that Kevetrin, but not paclitaxel, had potent anti-tumor activity against a human lung adenocarcinoma xenograft tumor model, NCI-H1975, at a dose and schedule that was well-tolerated as indicated no 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.