Abstract

**Methods for PPTP In Vivo Testing**

17-DMAG and/or its metabolite were administered at 12 hour intervals.

**Pharmacodynamic evaluation of the Hsp90 inhibitor 17-DMAG**

In Vitro Testing Procedures

- **Testing Methods**
  - The maximal inhibition values for 17-DMAG exceeded 90% for all of the PPTP panel, as illustrated below.
  - The median ECV values for the 4 rhabdomyosarcoma cell lines were lower than the median ECV values for the remaining lines in the panel (28% versus 52% of ECV, whereas the median ECV values for the 2 neuroblastoma cell lines (NB-EBc1, Rh30) were greater than the remaining lines in the panel (92%).

**Results**

- **Abstract**
  - 17-DMAG was uniformly active against the cell lines of the PPTP program standard operating procedures.
  - The maximal inhibition values for 17-DMAG exceeded 90% for all of the PPTP panel.

**Conclusion**

- **In Vitro Testing Procedures**
  - 17-DMAG produced its greatest antitumor activity against 10 of 12 evaluable solid tumor xenografts (1 of 2 ALL xenografts. Using the time to event measure of HSP90 inhibition and was antitumor activity because of the multiple HSP90 client proteins that are involved in cancer cell growth and survival.

- **In Vivo Activity**
  - 17-DMAG induced significant differences in EFS distribution (treated compared to controls) in 10/26 (38%) of the solid tumor models and 5/6 (82%) of the ALL models.

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