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The targeted cytotoxic prodrug, AQ4N, has comparable activity to standard of care agents in colon and pancreatic cancer models.

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Background

- AQ4N (banoxantrone) is a prodrug of a potent topoisomerase II inhibitor, AQ4
- Systemic toxicity of AQ4N is minimized due to lack of systemic bioreduction to AQ4
- AQ4N selectively accumulates tumors, lymphoid tissues, GI tract and pancreas where it is bioreduced to AQ4
- AQ4N is being studied in human Phase I studies in the US and Europe
- AQ4N is active in colon (HT-29) and pancreatic (BXPC-3) cancer cell lines in vitro as follows:

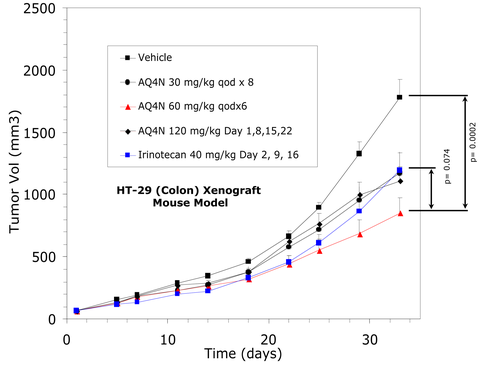
Tumor	Type	AQ4 (IC50)	AQ4N (IC50)*	Standard
HT-29	Colon	0.7 μM	101.5 μM	0.22 μM SN38 (irinotecan)
BXPC-3	Pancreatic	1.6 μM	3.6 μM	0.06 μM gemcitabine

*All studies done under normoxic conditions only

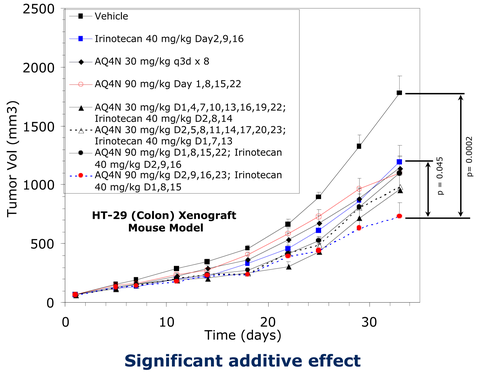
Methodology

- Tumor cells were implanted subcutaneously in Nu/Nu mice
- Tumors were allowed to grow to a mean size of 50-100 mm^3 prior to treatment
- Mice (8-10/group) were randomized to assure comparable inter-group mean tumor volumes at start of treatment
- AQ4N or irinotecan was injected intravenously and gemcitabine was administered intraperitoneally
- Several dose regimens of AQ4N were assessed
- AQ4N combination treatment with irinotecan was evaluated for dose sequence effects
- "Standard" doses of gemcitabine and irinotecan were used in these studies

AQ4N Comparable to Irinotecan

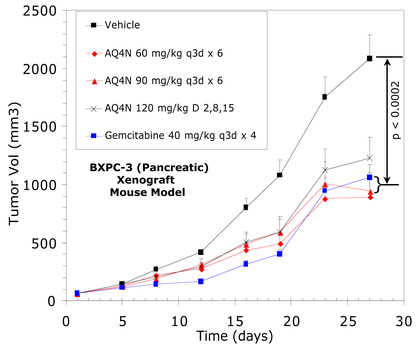


AQ4N + Irinotecan

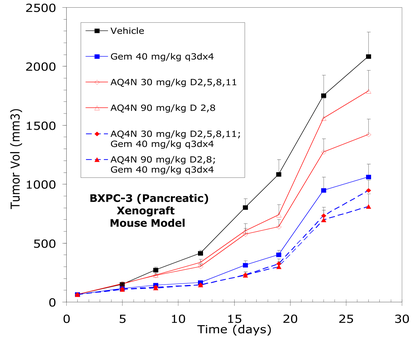


Significant additive effect

AQ4N Comparable to Gemcitabine



AQ4N + Gemcitabine



Summary

- AQ4N has a significant effect on tumor growth inhibition in colon (HT-29) and pancreatic (BXPC-3) xenograft models at 60 mg/kg (qod or q3d x 6)
- AQ4N has significant additive effect with irinotecan (AQ4N dosed after irinotecan)
- AQ4N may have additive effect with gemcitabine
- Data presented here has been replicated in another study at the optimal dose of AQ4N
- Studies are ongoing to confirm AQ4N activity in colon (HCT116) and pancreatic (Panc-1) xenograft models
- AQ4N distribution results indicate high levels of AQ4 in the GI tract and pancreas for 2 weeks after a single dose
- AQ4N may have utility in the treatment of pancreatic and colorectal cancer