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 SN38 | 0.22 μM SN38
BXPC-3 (Pancreatic) | 1.6 μM | 3.6 μM gemcitabine | 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 mm³ 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.

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.