The targeted cytotoxic prodrug, AQ4N, has anti-tumor efficacy in L1210, P388 murine leukemia and Namalwa human lymphoma 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 targets lymphatic tissues in vivo causing atrophy.
- AQ4N is active in Namalwa human lymphoma and L1210 and P388 murine leukemia cell lines as follows:

**Survival Benefit in Leukemia Models**

- AQ4N treatment yields long term survivors in L1210 leukemia model
- AQ4N treatment provides good survival benefit below MTD in P388 leukemia model
- Significant anti-tumor efficacy in Namalwa lymphoma xenograft model

**Methodology**

- The L1210 and P388 murine leukemia models were developed in DBA/2 mice (10-11 mice/group). Tumor inoculation was performed intraperitoneally (ip) on day 0, using 1 x 10^5 cells for L1210 and 1 x 10^6 cells for P388. Treatment was initiated ip on day 1, and efficacy was measured as percent survival. Treatment was compared with the standard agent, mitoxantrone.
- The Namalwa human lymphoma xenograft model was developed in nude mice (8-10 mice/group). Tumors were implanted subcutaneously. Drug treatment was initiated intravenously (iv) when established tumors were approximately 50-100 mm^3 in size. Anti-tumor efficacy was measured as tumor growth inhibition when control tumors reached appropriate size. Efficacy of AQ4N was compared to that of the standard agent, mitoxantrone.

**Significant Tumor Growth Inhibition**

- AQ4N treatment results in significant anti-tumor efficacy in three lymphoid tumor models, L1210, P388, Namalwa.
- In L1210 leukemia, AQ4N treatment resulted in 575% increased survival with 5/10 long term survivors.
- In P388 leukemia, AQ4N treatment resulted in 240% increased survival, similar to the standard agent mitoxantrone.
- In Namalwa lymphoma, AQ4N treatment resulted in significant tumor growth inhibition of 58%, again similar to mitoxantrone.
- AQ4N monotherapy in these models may be direct or indirect through AQ4; mechanistic studies are planned.

**Summary**

- AQ4N treatment results in significant anti-tumor efficacy in three lymphoid tumor models, L1210, P388, Namalwa.
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