BXQ-350: Modulating Ceramide and Sphingosine-1-Phosphate for Anti-Tumor Activity in Cancer Patients with Advanced Disease

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Background:
Sphingolipids are a class of bioactive signaling molecules implicated in multiple cellular processes and molecular pathways. Many publications have demonstrated that ceramides are proapoptotic while sphingosine-1-phosphate (S1P) activates multiple oncogenic pathways and stimulates immuno-suppressor cells promoting a pro-tumoral microenvironment. Several studies have shown high levels of ceramides being associated with improved survival, while high S1P levels are associated with a poor prognosis.

Method:
BXQ-350 is a nanovesicle of Saposin C, an allosteric activator of sphingolipid metabolism, that lowers systemic S1P and increases C18 ceramide. BXQ-350 was investigated in a Phase 1 dose-escalation safety study in an all-comer cancer patients with advanced solid malignancies (NCT02859857) to determine its safety profile and potential clinical activity as monotherapy. Samples were collected to explore potential biomarkers.

Results:
13 patients had potential clinical benefit up to cycle 6 (PR, SD), with the majority experiencing a decrease in systemic S1P levels and an increase in C18 levels. 8 patients (~11% of evaluable patients) with different solid tumor types (brain, CNS, H&N, CRC, GI) had PFS≥ 6 months, with 2 patients still on study six years after enrollment. Analysis of plasma samples also revealed an increase in anti-tumoral cytokines (IFNg, TNFa, IL-2) and a decrease in pro-tumoral ones (IL-6, 8, 10).

Conclusion:
Results of the Phase 1 study in heavily pretreated cancer patients indicate BXQ-350 was well tolerated and suggest BXQ-350 may provide a clinical benefit across multiple types of solid tumors. Both anti-tumor and anti-CIPN endpoints are being investigated in a phase 1b/2 trial of BXQ-350 in combination with FOLFOX7/Bevacizumab in newly diagnosed metastatic colorectal cancer patients.