BXQ-350: A NOVEL ANTI-CANCER BIOLOGIC AGENT THAT MAY MITIGATE CHEMOTHERAPY INDUCED PERIPHERAL NEUROPATHY

Background:

Chemotherapy Induced Peripheral Neuropathy (CIPN) is a frequent and debilitating side effect associated with the use of a wide range of antineoplastic agents, encompassing both cytotoxic and targeted agents. CIPN significantly impacts the quality of life of cancer patients undergoing treatment, potentially hindering clinical benefit. The underlying pathology of CIPN remains complex and incompletely elucidated. Emerging evidence suggests a link between altered neuronal sphingolipid metabolism and the development of neuropathic pain, while elevated plasma levels of sphingosine-1-phosphate (S1P) have also been observed in patients receiving chemotherapy who subsequently develop CIPN.

Method:

BXQ-350, a nanovesicle containing Saposin C, which is an allosteric activator of sphingolipid metabolism, has been shown to reduce systemic S1P levels. Additionally, it protects neurons and axons against the cytotoxic effects of various chemotherapeutic agents. BXQ-350 underwent evaluation in a Phase 1 dose-escalation safety study involving adult cancer patients with advanced solid malignancies who had previously undergone extensive treatment (ClinicalTrials.gov identifier: [NCT02859857](https://clinicaltrials.gov/show/NCT02859857)). Furthermore, its cytoprotective capabilities against several agents known to induce CIPN were investigated *in vitro*. *In vivo* experiments utilizing a CIPN preclinical model were conducted to explore BXQ-350's potential for protecting against CIPN.

Results:

Several patients with chronic CIPN at time of enrollment in the Phase 1 study anecdotally reported improvement of their neuropathic symptoms after receiving BXQ-350. Results from preclinical experiments revealed that BXQ-350 protected cells from oxaliplatin, paclitaxel, bortezomib or MMAE neurotoxicity. BXQ-350 was subsequently investigated in a murine oxaliplatin-induced CIPN preclinical model, and results demonstrated a dose-dependent reduction of mechanical allodynia correlating with decreasing systemic levels of S1P.

Conclusions:

Preclinical results demonstrated that BXQ-350 was highly effective at protecting neuronal cells and axons from antineoplastic agents known to induce CIPN and preventing CIPN in a murine preclinical model. These results support the clinical observation that BXQ-350 reduced symptoms of CIPN in several cancer patients. Additional clinical and pre-clinical studies are on-going.