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C 93

BXQ-350 may alleviate symptoms of chemotherapy-induced peripheral neuropathy via modulation of S1P

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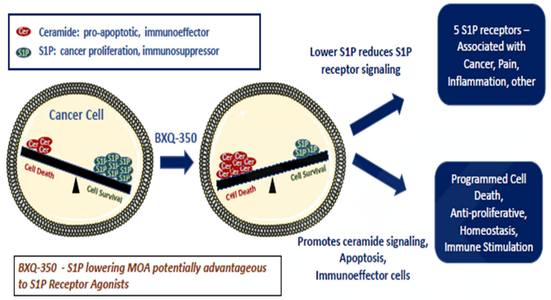
1. Background:

- **Chemotherapy-induced peripheral neuropathy (CIPN) is a significant side effect associated** with many chemotherapeutic agents.
- **CIPN is highly prevalent in CRC patients receiving therapeutic regimens including oxaliplatin;** ~15-20% of patients suffer from chronic CIPN that severely impacts quality of life (QoL) and may require dose vacation, dose reduction or treatment interruption.
- **CIPN's pathology is complex** and not completely understood; preclinical and clinical data has shown **inflammatory (IL-6, Il-8, IL-10) and immune involvement as well as increased levels of sphingoisine-1-phosphate** (S1P), a bioactive signaling sphingolipid
- **Elevated S1P and dysregulated sphingolipid metabolism are associated with many diseases** including cancer, autoimmune, inflammatory, Gaucher and Parkinson diseases

2. BXQ-350 is a nanovesicle formulation of Saposin C, an allosteric activator of sphingolipid metabolism that normalizes dysregulated sphingolipid metabolism by lowering S1P and increasing ceramides levels



3. Methods: BXQ-350 was investigated in

- ***in vitro* and *in vivo* preclinical CIPN models**

- **a Phase 1 dose escalation safety study in all-comer cancer patients** with recurrent solid malignancies (NCT02859857)
  - BXQ-350 was **safe and well-tolerated** (no Dose Limiting Toxicity); a **17.8% Clinical Benefit Rate** (CR, PR, SD) was observed at Cycle 6 (**see Poster C154**)
  - **One patient self-reported an improvement of her pre-existing CIPN symptoms** soon after BXQ-350 administration; this observation was confirmed in 4 out of 10 patients with established CIPN at the time of enrollment

Summary

- **BXQ-350 is a novel biologic** and a nanovesicle formulation of Saposin C, an allosteric activator of enzymes involved in sphingolipid metabolism
- BXQ-350 modulates sphingolipid metabolism**, lowers S1P and increases ceramide levels**
- BXQ-350 is **well-tolerated and showed signs of single agent activity in multiple tumor types** in patients with recurrent advanced disease (**See Poster C 154**)
- In preclinical models, BXQ-350 **protects neuronal cells from oxaliplatin's neurotoxicity and prevents oxaliplatin-induced CIPN in mice**
- Clinically**, BXQ-350 seems to resolve CIPN symptoms in some cancer patients**

On-going Studies

BXQ-350 is currently being investigated in:

- Phase 1/2 study in combination with SoC in newly diagnosed mCRC patients (NCT05322590)
- PoC and PK/PD study in cancer patients with established CIPN (NCT05291286)
- Phase 2 study in combination with radiation in pediatric DIPG/Diffuse Midline Glioma (NCT04771897)

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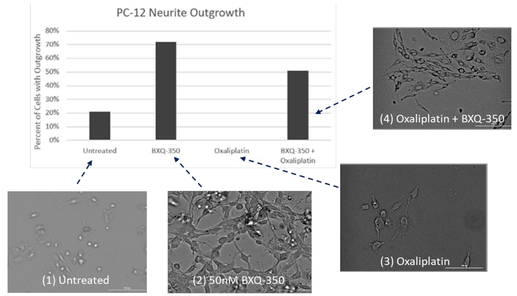
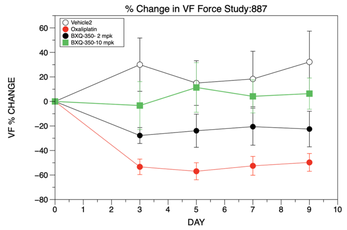
4. Preclinical Results:

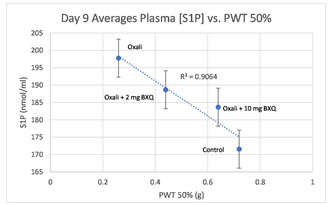
BXQ-350 protects

- PC12 neuronal cells from oxaliplatin's neurotoxicity and promotes neurite growth



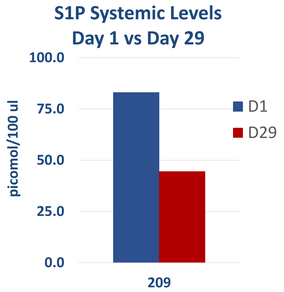
- mice from oxaliplatin-induced CIPN in a murine mechanical allodynia model



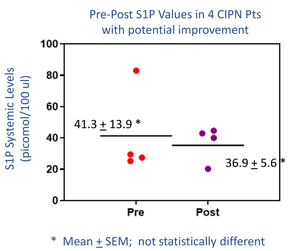


5. Clinical Results:

- Pancreatic cancer patient (209) with history of grade 2 CIPN (oxaliplatin & nab-paclitaxel) spontaneously reported resolution of her symptoms by Cycle 2



- Patients with known CIPN symptoms at enrollment were *a posteriori* asked about their symptoms after receiving BXQ-350:
  - 4 out 10 patients appeared to have improvements of their symptoms following BXQ-350 administration
  - S1P levels decreased post BXQ-350 in 6 out 10 patients



* Mean ± SEM; not statistically different