ASCO GI 2025

Trial in Progress:
A Phase 1b/2 Study on the Efficacy and Safety of BXQ-350 in Combination with mFOLFOX7 and Bevacizumab in Newly Diagnosed Metastatic Colorectal Cancer (mCRC) Patients

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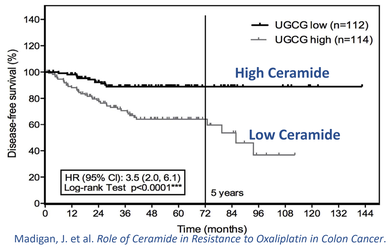
1. Background:

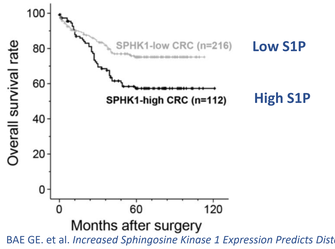
- **Sphingolipids are key signaling molecules in cancer**
- **Ceramides:** Pro-apoptotic; enhance anti-tumoral immunity
- **S1P:** Promotes tumor growth and pro-tumoral immunity
- **Elevated ceramide or low S1P levels are linked to better survival and prognosis in CRC patients**

Ceramide associated with improved survival GSE14333 CRC patients (n=226)



Madigan, J. et al. *Role of Ceramide in Resistance to Oxaliplatin in Colon Cancer.* Exp Cell Res , 2020, March 15, 388.

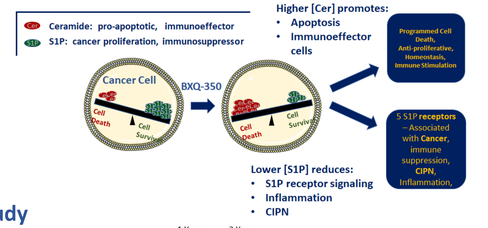
Low SPHK1 expression / Low S1P levels associated with better survival in CRC patient (n=328)



BAE GE. et al. *Increased Sphingosine Kinase 1 Expression Predicts Distant Metastasis and Poor Outcome in Patients with Colorectal Cancer.* Anti Cancer Research, 2019, 39:663-670.

2. BXQ-350 is a nanovesicle formulation of Saposin C, an allosteric activator of sphingolipid metabolism

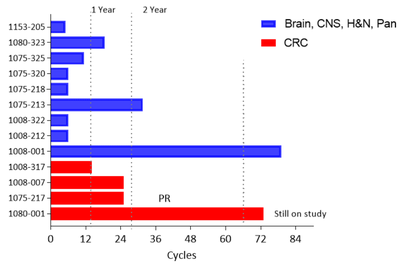
- normalizes dysregulated sphingolipid metabolism, lowering S1P and increasing ceramides levels



3. BXQ-350 was investigated in a Phase 1 study

with recurrent solid malignancies (NCT02859857)

- BXQ-350 was **safe and well-tolerated**
- **17.8% Clinical Benefit Rate** (PR, SD) observed at Cycle 6 across tumor types including CRC, appendiceal, pancreatic and rectal cancers
- **One patient self-reported improvement of pre-existing CIPN symptoms** soon after BXQ-350 administration



Summary

- **BXQ-350 is a novel biologic** and nanovesicle formulation of Saposin C, an allosteric activator of enzymes involved in sphingolipid metabolism
- BXQ-350 modulates sphingolipid metabolism**, lowering S1P and increasing ceramide levels**
- BXQ-350 is **well-tolerated and showed signs of single agent activity** across 20 refractory solid tumors types in a **Phase 1 study of 87 patients**
- **Potential biomarkers** based on S1P & ceramide, cytokines, PBMCs, ctDNA, NfLs
- **BXQ-350 may prevent or resolve CIPN**
- **DSMB review of safety data approved continuation**

Other Studies:

BXQ-350 is currently being investigated in:

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

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4. BXQ-350 + mFOLFOX7 & Bevacizumab study design:

Phase 1b/2 study in combination with mFOLFOX7 and Bevacizumab in newly diagnosed mCRC patients

- **Phase 1b/2:**
  - Safety dose escalation to establish RP2D. Patients started at 1.8 mg/kg BXQ-350 in combination with mFOLFOX7 and Bevacizumab; No MTD, BXQ-350 increased to 2.4 mg/kg which is now the RP2D.
  - 30 patient expansion cohort at the RP2D

Primary objectives Phase 1b/2:

- Select **RP2D** (safety profile, DLTs)
- **Preliminary efficacy** of the combination based on **ORR (Overall Response Rate), COD (Cumulative Oxaliplatin Dose)**

Secondary objectives Phase 1b/2:

- Overall safety and tolerability of combination
- Efficacy of BXQ-350 + mFOLFOX7 & Bevacizumab based on **DCR (Disease Control Rate), OS (Overall Survival), PFS (Progression Free Survival)**
- **Assess whether BXQ-350 decreases development, intensity or duration of CIPN** based on neuropathy scores from EORTC questionnaires (QLQ-C30 and CIPN20)

Exploratory objectives Phase 1b/2:

Potential correlation of PD biomarkers with response

- Immuno & sphingolipid profiling
- Neurofilament light chain (NfL) to monitor CIPN
- ctDNA analysis

Current Status:

- 3 patients enrolled at 1.8 mg/kg and 30 patients enrolled at 2.4 mg/kg
- DSMB reviewed the available safety data and approved continuation of enrollment
- Currently available safety data of the combination of mFOLFOX7 + Bevacizumab with BXQ-350 consistent with historical safety data for mFOLFOX7 + Bevacizumab

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