ASCO GI 2024
TPS 224
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Trial in Progress:
A Phase 1b/2 Placebo Controlled, Double Blinded Study on the Efficacy and Safety of BXQ-350 in Combination with mFOLFOX7 and Bevacizumab in Newly Diagnosed Metastatic Colorectal Carcinoma Patients

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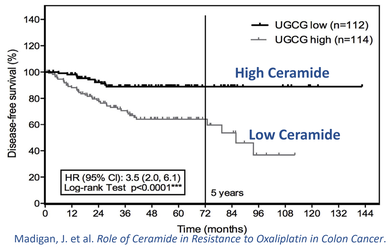
1. Background: Sphingolipids are bioactive signaling molecules implicated in cancer

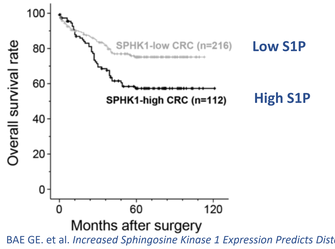
- **Ceramides** are pro-apoptotic and promote an anti-tumoral immune environment
- **Sphingosine-1-phosphate** (S1P) promotes tumor progression and a pro-tumoral immune environment
- **Several studies have shown elevated ceramide or low S1P levels** are associated with **improved survival and better 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.

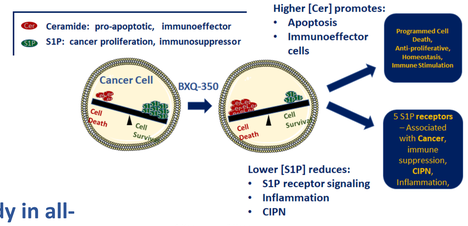
Low SPHK1 expression / Low S1P levels associated with better survival in CRC patient (n=328)



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.

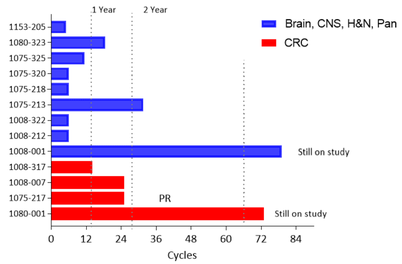
2. BXQ-350 is a nanovesicle formulation of Saposin C, an allosteric activator of sphingolipid metabolism

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



3. BXQ-350 was investigated in a Phase 1 study in all-comer cancer patients 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 a 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 in multiple tumor types** in patients with solid tumors refractory to standard therapies in a prior Phase 1 study
- **Potential biomarkers based on S1P & Cer**
- **BXQ-350 may prevent or resolve CIPN**
- **DSMB review of safety data approved continuation**

Other On-going 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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Acknowledgement: Patients who participated in the trials and their families, clinicians and staff at investigational sites, Bexion's personnel

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

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

- **Phase 1b:**
  - safety dose escalation to establish RP2D. Patients to start at 1.8 mg/kg BXQ-350 in combination with mFOLFOX7 and Bevacizumab; if no MTD, BXQ-350 will be increased to 2.4 mg/kg which would be the RP2D (if no MTD).
  - 30 patient expansion cohort at the RP2D
- **Phase 2:**
  - Up to 160 patients to be randomized 1:1 to receive BXQ-350 and mFOLFOX7-Bevacizumab combination or Placebo and mFOLFOX7-Bevacizumab

Primary objectives Phase 1b/2:

- Select **RP2D** (safety profile, DLTs)
- **Preliminary efficacy** of the combination based on **ORR**

Secondary objectives Phase 1b/2:

- Overall safety and tolerability of combination
- Efficacy of BXQ-350 + mFOLFOX7 & Bevacizumab based on ORR, PFS, duration of response and disease control rate
- Assess whether BXQ-350 decreases development, intensity or duration of CIPN based on neuropathy scores from EORTC questionnaires (QLQ-C30 and CIPN20)
- Assess whether BXQ-350 enables patients to receive a higher cumulative dose of oxaliplatin

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 18 patients enrolled at 2.4 mg/kg
- DSMB reviewed the available safety data on initial 12 patients and approved continuation of enrollment
- Currently available safety data of the combination with BXQ-350 appears similar to what is observed for mFOLFOX7 + Bevacizumab