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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

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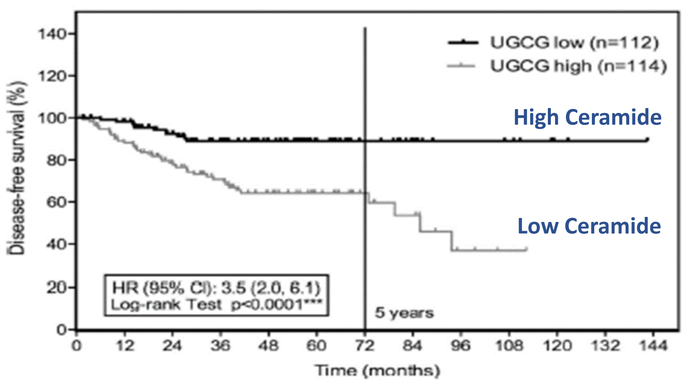
1. Sphingolipids are critical bioactive signaling molecules implicated in cancer:

- **Ceramides** are pro-apoptotic, mitigate resistance and promote an anti-tumoral immune environment
- **Sphingosine-1-phosphate** (S1P) promotes cancer cell proliferation, resistance, oncogenic pathways and a pro-tumoral immune environment
- **Elevated ceramide levels** are associated with **longer survival**

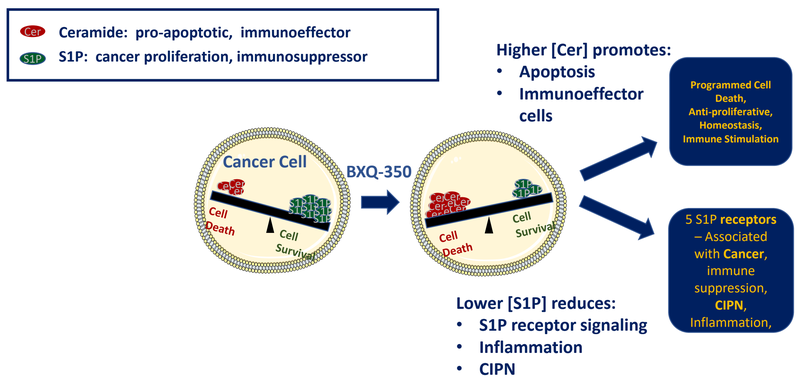
Ceramide associated with longer survival in Colorectal Carcinoma GSE14333 CRC patients (n=226)

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



2. BXQ-350 is a novel biologic modulating sphingolipid metabolism:

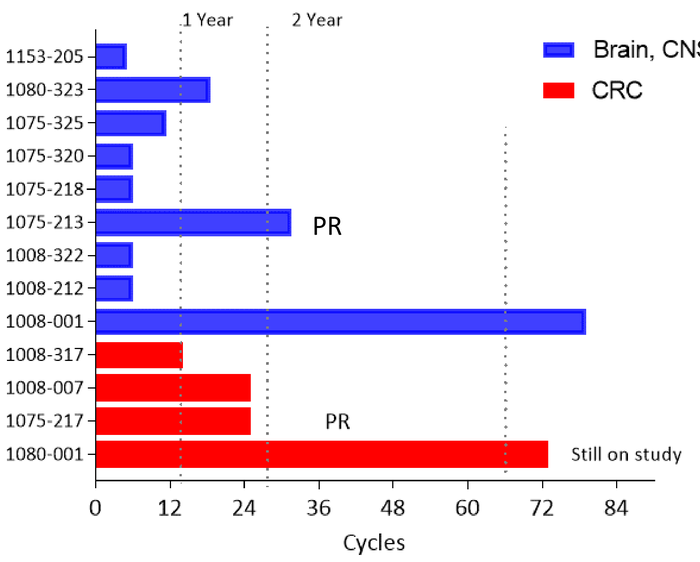
- Normalizes dysregulated sphingolipid metabolism in cancer, increasing Ceramide and lowering S1P levels



3. BXQ-350 was investigated in 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)
- **17.8% Clinical Benefit Rate** (CR, PR, SD) observed across tumor types including CRC, appendiceal, pancreatic and rectal cancers
- Multiple patients had long term clinical benefit
- **A patient self-reported an improvement of pre-existing CIPN symptoms,** observation corroborated by post analysis of other patients with CIPN at time of enrollment

Patients in Phase 1 Single Agent Study with PFS > 6 Months & Beyond



Summary

- **BXQ-350 is a novel biologic** that 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** including GI cancers
- **BXQ-350 may prevent or resolve CIPN**

Other Clinical 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:**
  - 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:

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

Primary objectives Phase 2:

- **Efficacy** of BXQ-350 + mFOLFOX7 & Bevacizumab based on **ORR and PFS**

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

5. Study status:

Enrollment in Phase 1b is ongoing:

- BXQ-350 @ 1.8 mg/kg: 3 of 3 patients enrolled; no DLT, no MTD. Data Safety Monitoring Board approved dose escalation
- BXQ-350 @ 2.4 mg/kg: 7 of 9 patients enrolled; no DLT, no MTD to date
- Study now opened at 15 US sites to complete enrollment @ 2.4 mg/kg and enroll 30 patients in expansion cohort