ASCO GI 2026
TPS 273
L7

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 Carcinoma Patients

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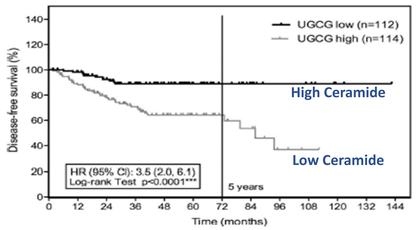
1. Background: Sphingolipids are bioactive signaling molecules implicated in cancer

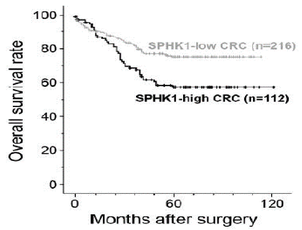
- **Ceramides** are pro-apoptotic and promote an anti-tumoral immune environment
- **Sphingosine-1-phosphate** (S1P) promotes progression and a pro-tumoral immune environment
- **Several studies have shown elevated ceramide or low S1P levels** are associated with **improved survival and better prognosis**

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.

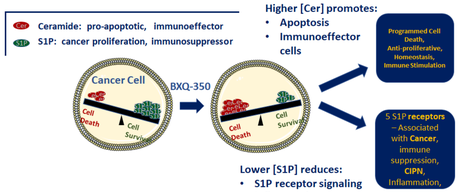
Low SPHK1 expression / Low S1P levels associated with better survival in CRC patient (n=328)



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.

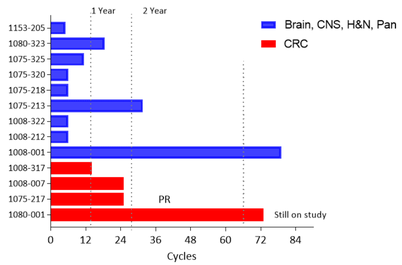
2. BXQ-350 is a nanovesicle formulation of Saposin C, an allosteric activator of sphingolipid metabolism

- 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 multiple 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, **lowers Gangliosides, LAcCer, GluCer, S1P and increases 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
- **Addition of BXQ-350 to SoC is well tolerated**
- **BXQ-350 may prevent CIPN**

Other Completed Trials:

- 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)
- Phase 1 study of BXQ-350 in adult patients with advanced Solid Tumors (NCT02859857)

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4. Phase 1b/2 study of BXQ-350 in combination with mFOLFOX7 and Bevacizumab in newly diagnosed mCRC patients

- 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:

- PD biomarkers; Immuno & sphingolipid profiling
- Neurofilament light chain (NfL) to monitor CIPN

Current Status:

- Enrollment completed and in active follow-up
- A total of 32 evaluable patients enrolled
- 30 patients (94%, all but 2 PD patients) achieved at least 8 cycles of oxaliplatin; 33% achieved at least 12 cycles.
- 94% of patients received > 6 cycles of oxaliplatin which is significantly higher than historical controls, 68% of patients ≥ 6 cycles of oxaliplatin (TRIBE and TRIBE 2 pooled analysis, R. Moretto *et al.*, Eur J Cancer 2025, 115470)
- Diseasce control rate (DCR) is 94% , ORR is 61% and mPFS is currently 10.6m
- Safety profile for the combination seems better than historical safety data for mFOLFOX7 + Bevacizumab, including CIPN

See Poster Board K2 / Abstract 242 for detailed safety and efficacy analysis
See Poster Board D17 / Abstract 105 for detailed CIPN analysis

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