AACR 2026
Session CL01.04
Poster 3737/9

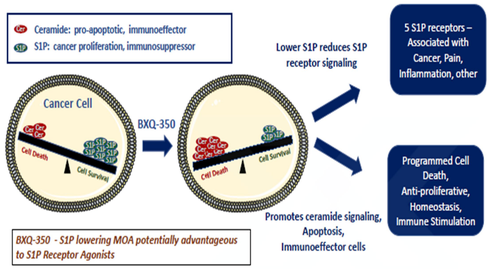
BXQ-350: A Novel Biologic that Targets Dysregulated Sphingolipid Metabolism and Normalizes Key Pro / Anti Tumoral Sphingolipids in Newly Diagnosed Metastatic Colorectal Cancer Patients

G. Tapolsky, T. Arshad, J. Beach, J. Bond, M. Gazda, N. Wilkins

Bexion Pharmaceuticals, Covington, KY, USA

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

- Activates glucosylcerebrosidase (Gcase) and normalizes dysregulated sphingolipid metabolism, **lowering S1P and increasing ceramides levels**
- **Modulates S1P signaling & stimulates immune response**

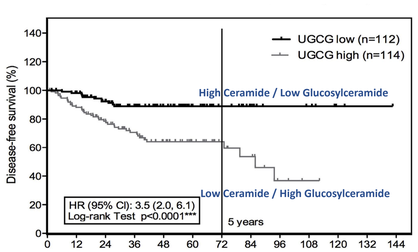


2. Sphingolipids are bioactive signaling molecules implicated in cancer

- **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
- **Several studies have shown elevated ceramide levels** are associated with **improved survival**

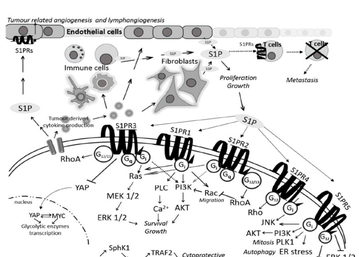
Ceramide associated with improved survival GSE14333 CRC patients (n=226)

Madigan, J. et al. Exp Cell Res , 2020, March 15, 388.



S1P signaling activates multiple oncogenes and induces a pro-tumoral immunosuppressive environment

Grbcic, P. et al. *S1P Signaling and Metabolism in Colon Cancer*. Molecules, 2020, 25, 2436



3. Phase 1b/2 study: BXQ-350 in combination with mFOLFOX7 + Bevacizumab in newly diagnosed mCRC patients (NCT 05322590):

- 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 increased to 2.4 mg/kg which would be the RP2D (if no MTD).
- 30 patient expansion cohort at the RP2D

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 dysregulated sphingolipid metabolism, lowers S1P and increases ceramide levels promoting a return to homeostasis**
- 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
- BXQ-350 is **well-tolerated in combination with mFOLFOX7 + bevacizumab in 1L mCRC patients:**
  - Disease control rate (DCR) is 91%, ORR is 61% and mPFS is currently 10.6m
  - Safety profile for the combination appears better than historical safety data for mFOLFOX7 + Bevacizumab, including CIPN
- **Biomarkers based on plasma S1P & Cer, Glu, NfL and cytokines**
- **Potential association between Cer/S1P and survival**
- **Potential association between Glu and BOR**
- **BXQ-350 may prevent and resolve CIPN**

Other Completed Trials:

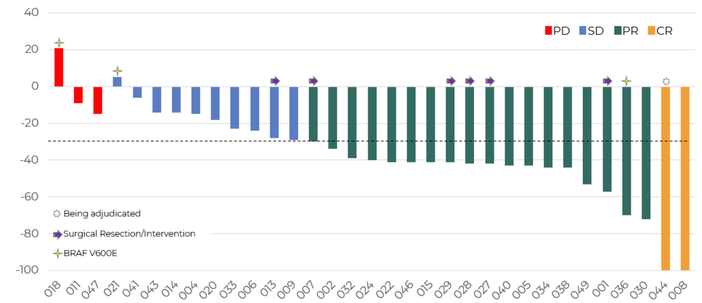
- PoC and PK/PD study in cancer patients with established CIPN (NCT05291286)
- Phase 1 study in combination with radiation in pediatric DIPG/DMG patients (NCT04771897)
- Phase 1 study of BXQ-350 in adult patients with advanced Solid Tumors (NCT02859857)

Related Posters at AACR 2026:

- **Session PO.CTP01.01 Poster CT084/15** A Phase 1b/2a study to evaluate the efficacy and safety of BXQ-350 in combination with mFOLFOX7 and bevacizumab in newly diagnosed metastatic colorectal carcinoma patients (mCRC): Evidence of lower incidence and severity of CIPN events.
- **Session PO.CTP01.03 Poster CT220/15** A Phase 1b/2a study to evaluate the efficacy and safety of BXQ-350 in combination with mFOLFOX7 and bevacizumab in newly diagnosed metastatic colorectal carcinoma patients (mCRC): Interim efficacy subset analyses.
- **Session PO.PR01.04 Poster 3616/2** BXQ-350 reduces incidence, severity, and time to on-set of chemotherapy induced peripheral neuropathy via modulation of sphingolipid metabolism.

Acknowledgement: Patients who participated in the trials and their families, clinicians and staff at investigational sites, and Bexion personnel.

Tumor Change from Baseline



ORR 61%
DCR 91%
mPFS 10.6 months

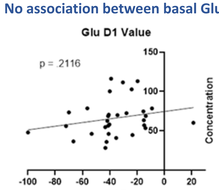
- 5 of these patients left study to receive surgical resection of their tumors
- 2 additional patients left study early for surgical resection (1 PR, 1 SD, both not evaluable)
- 1 patient (029) received radioembolization treatment of liver lesion

The data are provisional and are subject to change based on future updates.

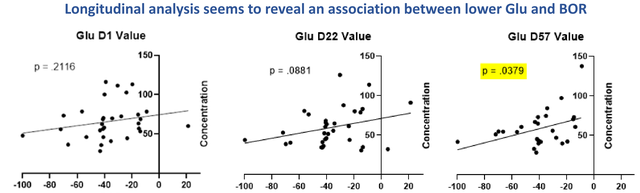
4. Trends in basal and longitudinal sphingolipids levels after BXQ-350 + SoC

Glucosylceramide (Glu) levels and Best Overall Response (BOR)

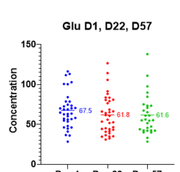
No association between basal Glu & BOR

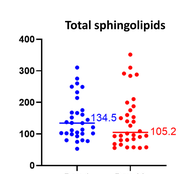


Longitudinal analysis seems to reveal an association between lower Glu and BOR

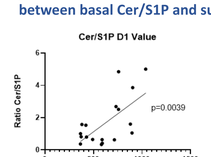


Longitudinal analysis suggests that Glu levels decrease over time as well as total sphingolipids





Cer/S1P and survival: Potential association between basal Cer/S1P and survival



Longitudinal analysis seems to confirm association between Cer/S1P and survival