ASCO GI 2023
C 154

BXQ-350: modulating ceramide and S1P for anti-tumor activity in CRC patients with advanced disease

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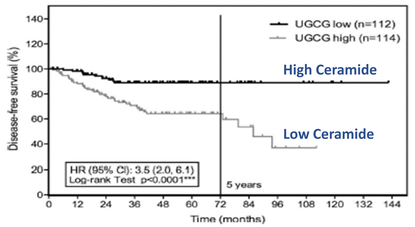
1. Background: Sphingolipids are bioactive signaling molecules implicated in cancer

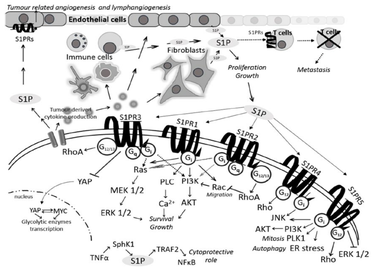
- **Ceramides** are pro-apoptotic, mitigate resistance and promote an anti-tumoral immune environment
- **Sphingosine-1-phosphate** (S1P) promotes cancer cell proliferation, resistance, oncogenic pathways and a pro-tumoral immune environment
- **Several studies have shown elevated ceramide levels** are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

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



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

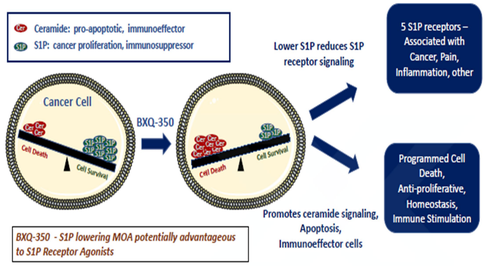
S1P signaling activates multiple oncogenes and induces a pro-tumoral immunosuppressive environment



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

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
- modulates S1P signaling & stimulates immune response



3. Method: 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) was observed at Cycle 6 across tumor types including CRC, appendiceal, pancreatic and rectal cancers
- **One patient self-reported an improvement of pre-existing CIPN symptoms** soon after BXQ-350 administration (see Poster C 93)

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 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
- **Potential biomarkers based on S1P & Cer**
- **BXQ-350 may resolve CIPN symptoms in some cancer patients (See poster C 93)**

On-going Studies

BXQ-350 is currently being investigated in:

- Phase 1/2 study in combination with SoC in newly diagnosed mCRC patients (NCT05322590)
- PoC and PK/PD study in cancer patients with established CIPN (NCT05291286)
- Phase 2 study in combination with radiation in pediatric DIPG/Diffuse Midline Glioma patients (NCT04771897)

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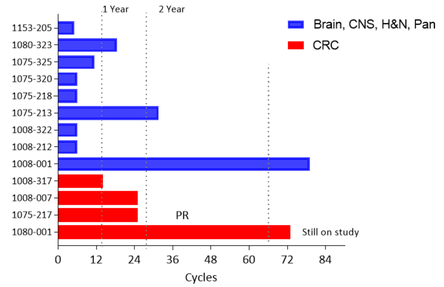
Acknowledgement: Patients who participated in the trials and their families, clinicians and staff at investigational sites, Bexion's personnel

4. Phase 1 Results:

PFS > 6, 12, 24, 60 months …

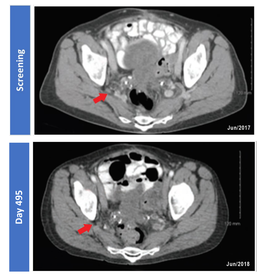
- 13 SD / PR patients PFS ≥ Cycle 6 (17% of evaluable pts with clinical benefit)
- Of the 13 pts with **PFS ≥ 6 months, 4 CRC patients including**
  - **a PR**
  - **a patient still on study after > 5 years**



PR

Pt 1008-007: 62-yr old female with mucinous adenocarcinoma of the appendix (stage IV)

- Diagnosed in May 2006 previously treated with surgery, chemotherapy and radiation
- Rapid progression (4 months) prior to starting BXQ-350
- **PR (-32%) and progressed after 743 days on BXQ-350**



Long lasting clinical benefit: Pt 1080-001 > 5 years on study

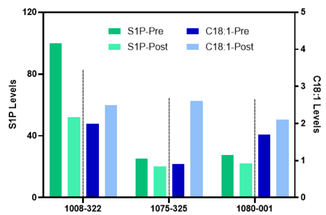
40-yr old female with stage IV mCRC

- Diagnosed in Nov 2005 previously treated with surgery, chemotherapy and radiation
- Raid progression (5 months) prior to starting BXQ-350
- Following Pre & Post S1P/C18:1 ratios as potential biomarkers

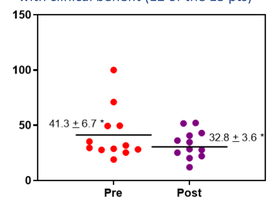
Pre-Post S1P & C18 values: MOA and response biomarkers?

- Further analysis needed in larger and tumor specific studies

Changes in Systemic C18:1 & S1P Levels



Pre-Post (Day 29) S1P/C18:1 in the 13 patients with clinical benefit (12 of the 13 pts)



- Mean ± SEM
- P= 0.281; not statistically different