AACR 2024
3072

BXQ-350: A Novel Biologic that Allosterically Activates Glucosylcerebrosidase and Demonstrates Promising Signs of Activity in Cancer Patients

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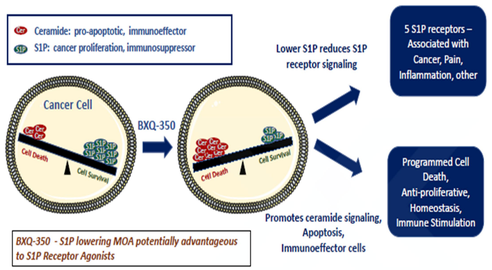
1. BXQ-350 is a nanovesicle formulation of Saposin C, an allosteric activator of sphingolipid metabolism

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

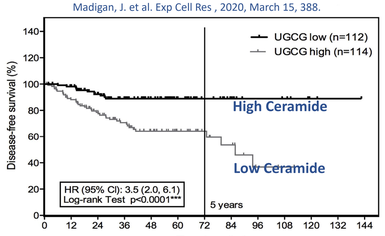


2. Sphingolipids are bioactive signaling molecules implicated in cancer

- **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**

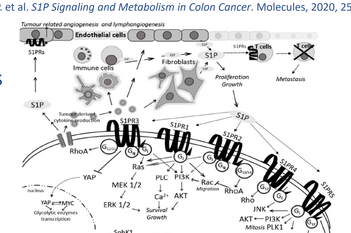
Ceramide associated with improved survival GSE14333 CRC patients (n=226)

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. In preclinical studies, BXQ-350 :

- lowers tissue glucosylceramides and increases ceramides
- increases C18 and lowers S1P across cancer cell lines
- is additive or synergistic with antineoplastic agents
- inhibits MDSCs, expands CD3+, CD4+ & CD8+ T cells, NK cells, repolarizes macrophages

4. 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**
- **had a 17.8% Clinical Benefit Rate** at Cycle 6 across tumor types including GBM, brain, CRC, appendiceal, pancreatic and rectal cancers; two patients are still on study with no evidence of disease after > 6 years of treatment

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 **disengages S1P signaling and rebalances the tumor microenvironment** towards an anti-tumoral state
- In clinical studies, BXQ-350 is **well-tolerated and showed promising signs of single agent activity in multiple tumor types**
- Investigating systemic levels of S1P and Ceramides as **potential biomarkers**
- BXQ-350 **may resolve CIPN symptoms in some cancer patients**
- **On-going preclinical studies to further elucidate BXQ-350's mechanism of action**

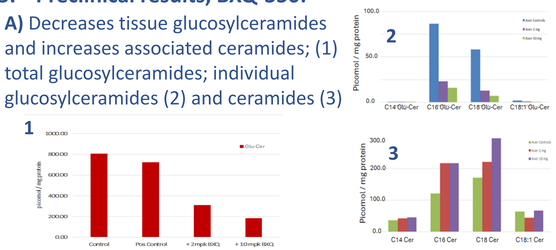
BXQ-350 is clinically being investigated in:

- Phase 1b/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 1 study in combination with radiation in pediatric DIPG/DMG patients (NCT04771897)

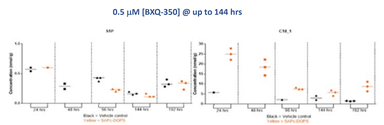
Acknowledgement: Patients who participated in the trials and their families, clinicians and staff at investigational sites, Bexion's personnel

5. Preclinical results, BXQ-350:

A) Decreases tissue glucosylceramides and increases associated ceramides; (1) total glucosylceramides; individual glucosylceramides (2) and ceramides (3)

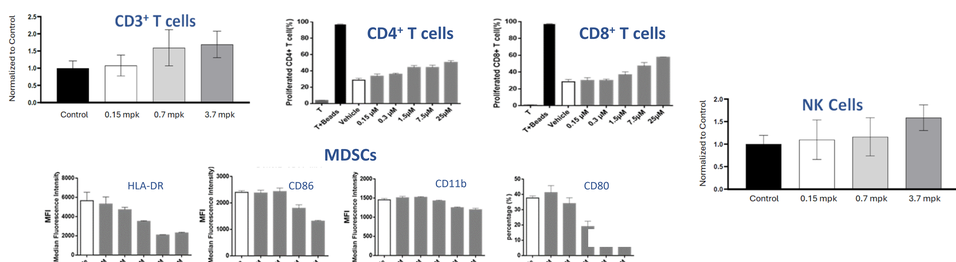


B) Decreases intracellular S1P & increases C18:1 across cancer cell lines



	Control	24 hrs	96 hrs	196 hrs
S1P/C18:1	0.11	0.06	0.03	0.03

C) Impacts immuno-effector/suppressor cells *ex vivo* and *in vivo*: CD3+ Tcells, CD4+/8+ Tcells, NK cells, MDSCs.



6. Phase 1 Safety & Dose Escalation Clinical Study Results (NCT02859857):

PFS ≥ 6, 12, 24, 60 months …

- **13 SD / PR patients PFS ≥ Cycle 6** (17.8 % of evaluable pts with clinical benefit) in GBM, CNS, GI and H&N cancers
- **7 patients with PFS ≥ 12 months**
- Changes in systemic levels of S1P or C18 ceramides in most patients with clinical benefit

Long lasting clinical benefit:

- **1 GBM and 1 CRC still on study after 7 years**