AACR 2026
Session PO.PR01.04
Poster 3616/2

BXQ-350, a First-in-class Sphingolipid Metabolism Modulator, Reduces Incidence, Severity and Time to On-set of Chemotherapy Induced Peripheral Neuropathy in Newly Diagnosed Metastatic Colorectal Cancer Treated with BXQ-350 and mFOLFOX7+bevacizumab

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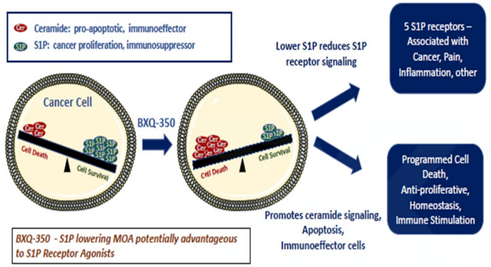
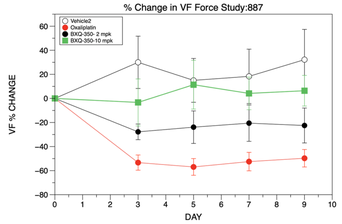
1. Background:

- **Chemotherapy-induced peripheral neuropathy (CIPN) is a significant side effect** associated with many chemotherapeutic agents.
- **CIPN is highly prevalent in CRC patients receiving therapeutic regimens including oxaliplatin;** ~15-20% of patients suffer from chronic CIPN severely impacting their quality of life (QoL) and may require treatment interruption.
- **CIPN's pathology is complex**; preclinical and clinical data has shown **inflammatory (IL-6, Il-8, IL-10) and immune involvement**
- **Dysregulated sphingolipid metabolism** is associated with many diseases including cancer and CIPN



2. BXQ-350 Preclinical Data:

- **BXQ-350 protects and rescues neurons** from chemotherapeutic agents' neurotoxicity promoting neuronal and axonal metabolism and growth
- **BXQ-350 protects from oxaliplatin-induced CIPN** in a murine mechanical allodynia model in a dose-dependent manner



3. Methods:

- **BXQ-350 is being investigated in a Phase 1b/2 study in combination with mFOLFOX7 and Bevacizumab (SoC) in newly diagnosed mCRC patients (NCT05322590) to assess the efficacy and safety of BXQ-350**.
- Phase 1b is an open label safety dose escalation to establish the RP2D exploring 1.8 and 2.4 mg/kg BXQ-350 in combination with SoC. At 2.4 mg/kg (no DLT), 9 patients were safely dosed, then additional patients were dosed to complete a 30-patient expansion cohort.
- Primary objectives are to assess safety and preliminary efficacy of BXQ-350 in this combination, to include determining cumulative oxaliplatin dose. A secondary objective is to determine if BXQ-350 decreases intensity, frequency, and/or delays on-set of CIPN.

4. Results:

- Key findings are reduction in incidence and delay in development of severe neuropathies, while enabling an increase in the total dose administered of oxaliplatin.

Study	% 6+ Doses Oxaliplatin	% <6 Doses Oxaliplatin
TRIBE2	68	32
Bexion Study	**94**	**6**

Cycles Dosed	Bexion % vs RWE
C8	85% vs 50%
C10	76% vs 25%
C12	58% vs 20%
>C12	27% vs 10%

Grade CIPN	Bexion % vs RWE
G2	36% vs 50%
G3	12% vs 18%
C10 G2	28% vs 50%
C12 G3	6% vs 48%

RWE References: ELOXATIN® USPI, Giantonio 2007, Tsai 2016, Kang 2023, Weickhardt 2011, deGramont 2007, Loprinzi 2014, Cremolini 2020, 2025, Rivera, 2017 Saltz 2008

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 may prevent and resolve CIPN**
- 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 **reduced incidence and/or severity of CIPN.**
- **Biomarkers** based on plasma levels of S1P & Ceramide, Cytokines, PBMCs, and NfLs.

Other Completed Trials:

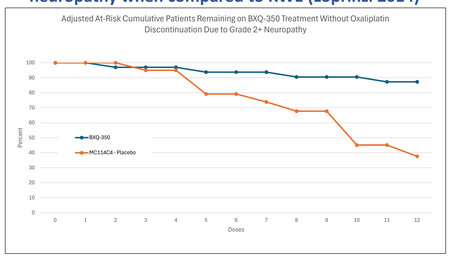
- PoC and PK/PD study in cancer patients with established CIPN (NCT05291286)
- Phase 1 study in combination with radiation in pediatric DIPG/DMG patients (NCT04771897)
- Phase 1 study of BXQ-350 in adult patients with advanced Solid Tumors (NCT02859857)

Related Posters at AACR 2026:

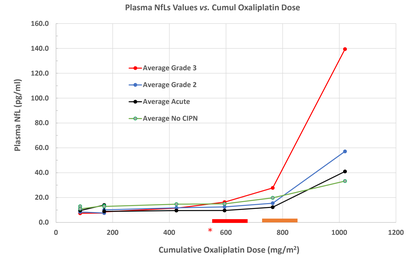
- **Session PO.CTP01.01 Poster CT084/15** A Phase 1b/2a study to evaluate the efficacy and safety of BXQ-350 in combination with mFOLFOX7 and bevacizumab in newly diagnosed metastatic colorectal carcinoma patients (mCRC): Evidence of lower incidence and severity of CIPN events.
- **Session PO.CTP01.03 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 CL01.04 Poster 3737/9** BXQ-350: A novel biologic that targets dysregulated sphingolipid metabolism and normalizes key anti-tumoral and pro-tumoral sphingolipids in newly diagnosed metastatic colorectal carcinoma patients (mCRC).

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

Far fewer subjects halted oxaliplatin dosing due to G2/3 neuropathy when compared to RWE (Loprinzi 2014)

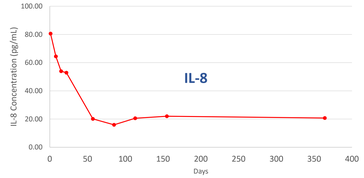


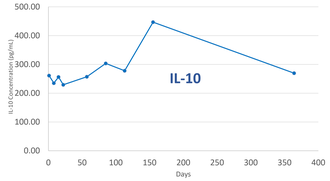
Plasma NfL tracked with Investigator graded neuropathy and show fewer G3 at C12 (6%), and later on-set vs RWE (*Cersosimo 2004)



5. Plasma Biomarkers:

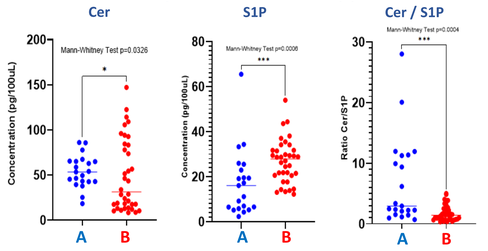
- **Pro and anti-inflammatory cytokines:** no longitudinal trends observed in cancer-free patients with chronic CIPN; **significant changes in mCRC patients receiving BXQ-350: decrease in IL-8** (a pro-inflammatory cytokine) **and increase in IL-10** (an anti-inflammatory cytokine)





- **Sphingolipid profiling:** BXQ-350 affects dysregulated sphingolipid metabolism and promotes a return to homeostasis. Basal levels and longitudinal changes appear to be different between cancer-free patients with chronic CIPN (no systemic disease) and mCRC patients (systemic disease)

Ceramide (Cer) and S1P basal plasma levels are different between cancer-free patients with chronic CIPN (A) and mCRC patients before treatment (B)



Changes in sphingolipid profiles after BXQ-350 appear to be different between cancer-free patients with chronic CIPN and mCRC patients

Total sphingolipid metabolism activity
(Sum of glucosylceramides, ceramides, sphingosine and S1P)
Seems to increase in CIPN patients & to decrease in mCRC patients