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Poster EPEN-14

BXQ-350 Shows Signs of Potential Activity in Ependymoma Patients

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1. Background:

Ceramides and Sphingosine-1-Phosphate (S1P) are sphingolipids, a class of bioactive signaling lipids implicated in many cancer related cellular pathways and cellular processes [1]:

- Ceramides are pro-apoptotic, down regulate oncogenic pathways and stimulate immuno-effector cells
- S1P promotes proliferation of cancer cells, activates oncogenic pathways, and stimulates immuno-suppressor cells.

Pediatric and adult ependymomas are heterogenous tumors; nonetheless, recent studies suggest:

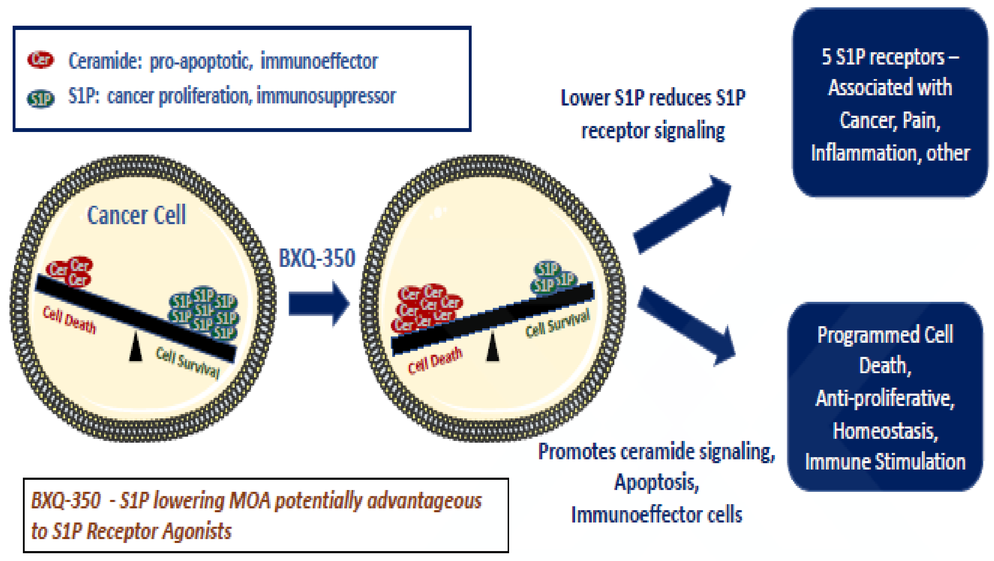
- NF2, Notch, hTERT predominantly associated to tumorigenesis [2]
- Co-amplification of S1P-Receptor 3 and SHC3 in ~60% of ependymomas [3]

➢ S1P signaling is associated with these oncogenic drivers [4]

(1) A. Janneh et al. , Targeting Sphingolipid Metabolism as a Therapeutic Strategy in Cancer, *Cancers* 2022, 14, 2183.
(2) Y. Yao et al. Molecular genetics of ependymoma, *Chinese Journal of Cancer,* 2011, vol 30 (10), 669.
(3) L. Magrassi et al, S1PR3 and SHC3 on chromosome 22 q are coamplified in human ependymomas, *Cancer Letters* , 2010, April, 290(1), 36.
(4) a) M Sheridan et al., The Role of Ceramide Metabolism and Signaling in the Regulation of Mitophagy and Cancer Therapy, Cancers, 2021, 13, 2475, b) R Watters et al. Targeting S1P Receptors in Cancer, *Anticancer Agents Med Chem. 2011* November ; 11(9): 810–817; c) N. Hirata et al., Sphingosine-1-phosphate promotes expansion of cancer stem cells via S1PR3 by a ligand-independent Notch activation, *Nature Communications*, 2014, 5:4806 | DOI: 10.1038, d)

2. BXQ-350:

BXQ-350 is a nanovesicle formulation of Saposin C, an allosteric activator of sphingolipid metabolism, and dioleoyl-phosphatidylserine (DOPS).



3. Ependymoma Patients:

Four ependymoma patients were enrolled in an adult dose Phase 1 study (NCT0285987): Patients 1075-218 and 1153-205 had partial responses (PR) in 1 of their target lesions (RANO), 1008-212 had stable disease (SD) up to Cycle 6, and 1080-324 experienced progressive disease (PD).

1075-218	1153-205	1008-212	1080-324
67 M	43 M	55 F	40 M
Grade III	Grade III	Grade II	Grade I
Brain	Brain	Spine	Brain
Initial diagnosis 2015	Initial diagnosis 2014	Initial diagnosis 2005	Initial diagnosis 2008
Chemo Radiation Surgery	Chemo Radiation Surgery	Radiation Chemo Surgeries	Chemo Radiation Surgery
Rapid progression prior to start on Dec 2018	Rapid progression prior start on Sept 2017	Rapid progression prior start on July 2018	Rapid progression prior start on May 2019
PR in 1 lesion PD Cycle 4	PR in 1 lesion PD Cycle 6	SD PD Cycle 6	PD Cycle 1

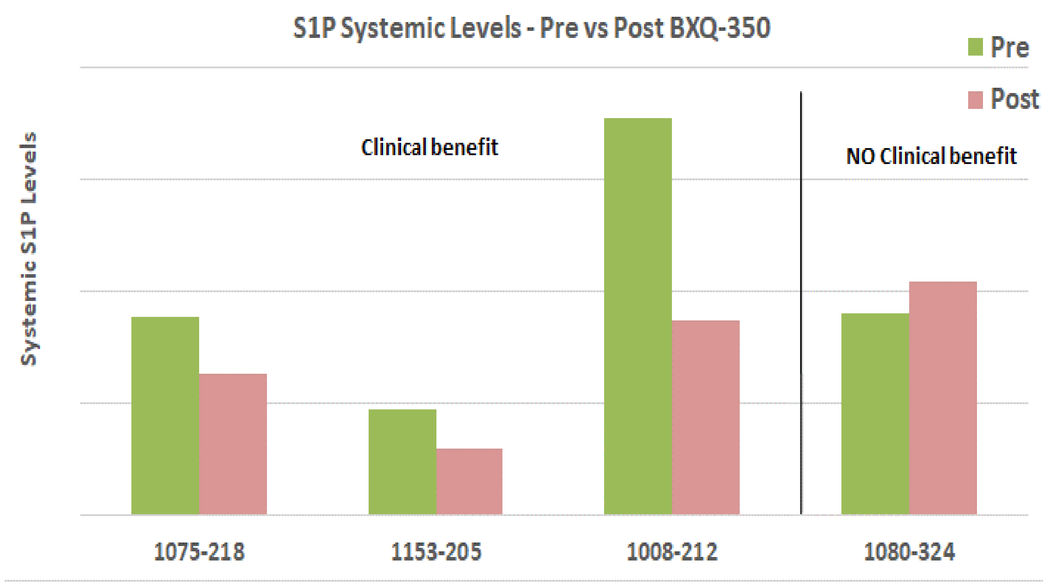
1075-218 Lesions Measurements

	Target Lesion #1	Target Lesion #2
	Brain L f l	Brain L f l
Screening	2.5	1.2
Cycle 2	2.2	0.7
Cycle 3	2.8	-
Cycle 4	3.5	0.9

1153-205 Lesions Measurements

	Target Lesion #1	Target Lesion #2
	Brain Intra Cra	Brain Ex Axial
Screening	6.4	3.2
Cycle 1	6.4	2.6
Cycle 2	6.7	2.1
Cycle 4	6.9	1.8
Cycle 5	8.4	1.8

Significant decrease in S1P in all patients with clinical benefit (regression in a lesion or SD)



4. BXQ-350 Clinical Studies:

- A Phase 1 dose-escalation safety study in adult all-comers cancer patients with advanced solid malignancies (NCT02859857); ependymoma patients described here were part of that study
- A Phase 1 dose-escalation safety study in pediatric patients with brain malignancies (NCT03967093)
- An on-going Phase 1/2 study in combination with radiation in pediatric DMG/DIPG patients (NCT04771897; see Poster DIPG-30)

5. BXQ-350 Safety Profile (adult all-comers study):

- BXQ-350 is safe and well-tolerated
- No DLT observed and a MTD was not reached
- The three most common adverse events reported are fatigue, nausea and flushing/infusion reactions

6. BXQ-350 Efficacy Profile (adult all-comers study):

- 11 patients (~15% of evaluable patients) had a potential clinical benefit
- 8 patients had a PFS > 6 months across different tumor types (including 2 GBM, 1 choroid plexus carcinoma)
- 2 patients (GBM, Colorectal) are still on study >5 years

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