Abstract #296359: A Pediatric and Young Adult Phase I Dose Escalation Safety Study of BXQ-350 for Refractory Solid and Central Nervous System Tumors

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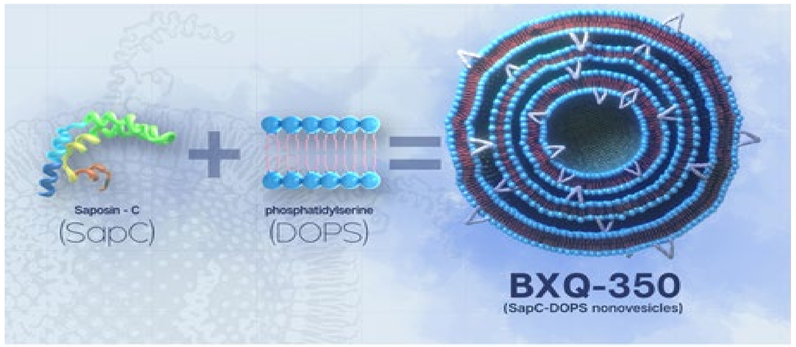
Introduction:

BXQ-350 is a novel anti-tumor agent in development from Bexion Pharmaceuticals, Inc. Composed of the multifunctional, lysosomal activator protein Saposin C (SapC) and dioleoyl- phosphatidylserine (DOPS), BXQ-350 has demonstrated antitumor effects in both in vitro and in vivo preclinical models. Many tumors, including high-grade glioma (HGG) and diffuse intrinsic pontine glioma (DIPG), and cells of tumor vasculature have aberrantly exposed phosphatidylserine (PS)-rich domains on the cell surface. BXQ-350 selectively targets tumor cell PS, particularly those translocated to the outer leaflet of the plasma membrane in tumor cells. Furthermore, BXQ-350 activates and participates in various cellular processes, including apoptosis and necrosis, and may also exhibit novel mechanisms leading to cell death that require further investigation.



Methods and Study Design:

A Phase I first-in-pediatric, dose escalation study of BXQ-350 (NCT03967093) for refractory solid and central nervous system (CNS) tumors was conducted at 2 sites in 2019. The primary objective of the study was to characterize the safety profile and determine the maximum tolerated dose (MTD) of BXQ-350. The MTD was defined as the highest dose level (DL) in which a dose limiting toxicity (DLT) was observed in <1 of 6 patients. Sequential single patient cohorts were administered BXQ-350 intravenously as outlined in the charts below:

Cohort	Dose (mg/kg)
DL 1	1.8
DL 2	2.4
DL 3	3.2

Cycle 1
Dose on Day:
Day 1-5
Day 8
Day 10
Day 12
Day 15
Day 22

→ **Cycle 2 and Beyond**
Every 28 days until study end or progression/ withdrawl

Results:

Analysis of the data is currently underway. Results are based on preliminary information known as of 24APR2020. The study enrolled one patient each at DL 1 and 2 and seven at DL 3 for a total of nine patients (2 non-CNS; 7 CNS) between the ages of 4 and 23 years. One osteosarcoma patient in DL 3 had progressive disease prior to completing cycle one of treatment and was replaced in order to meet the minimum requirements for establishing MTD. Eight patients (DIPG-3, HGG-1, Glioblastoma-1, Pineoblasotoma-1, Ependymoma-1, Osteosarcoma-1) completed an average of 2 cycles each, with one of the DIPG patients completing cycle five. There were no BXQ-350-related withdrawals, serious adverse events (SAEs), or DLTs. Therefore, the highest planned dose of 3.2 mg/kg was achieved safely but a maximum tolerated dose was not established A total of 305 treatment emergent adverse events (AEs) were noted ranging in severity from Grade 1 to 5 (287 AEs; 18 SAEs). The highest assigned relationship to BXQ-350 was "possibly related" and applied to only 11 AEs, as shown in the table below.

Possibly Related AEs	# Events	# Patients	% Patients (N=9)
Fatigue	4	3	33.3%
Nausea	2	2	22.2%
Hypertension	1	1	11.1%
Vomiting	1	1	11.1%
Creatinine increased	1	1	11.1%
Pneumonia	1	1	11.1%
Proteinuria	1	1	11.1%

Conclusion

BXQ-350 was well tolerated at all dose levels. Escalation to the highest planned dose level of 3.2mg/kg was safely achieved with no BXQ-350-related dose-limiting toxicities or SAEs. A pediatric Phase I trial in newly diagnosed DIPG patients is planned for 3rd quarter 2020.

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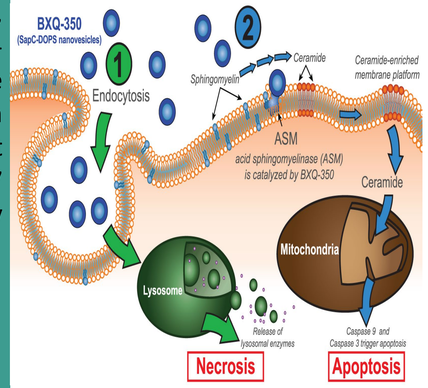
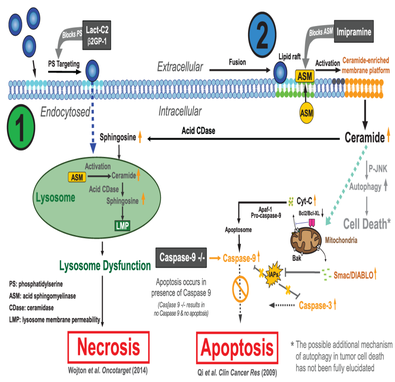
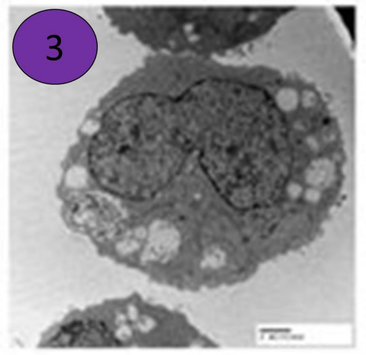
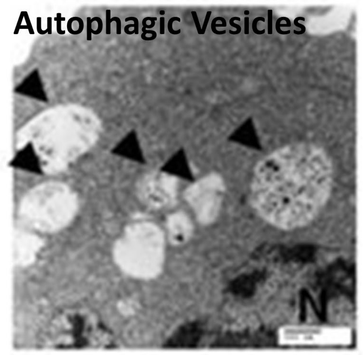
BXQ-350 Mechanism of Action

BXQ-350 is a sphingolipid modulator that induces cell death through three mechanisms: Mechanism 1 leads to necrosis through endocytosis of BXQ-350 and lysosomal degradation. Mechanism 2 leads to apoptosis by catalyzing acid sphingomyelinase to create ceramide. Mechanism 3 is an autophagic cell death via overproduction of autophagic vesicles.









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