Outcomes of High-Grade Glioma Patients in a Phase 1 Trial of BXQ-350, Cancer-selective SapC-DOPS Nanovesicles

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BACKGROUND

- BXQ-350 (Saposin C-dioleylphosphatidylserine, SapC-DOPS) is a novel blood-brain barrier penetrant nanovesicle agent that targets externalized phosphatidylserine overexpressed on tumor cell membranes. (Figure 1 and Figure 2)
- In a recent Phase 1a trial (NCT02859857), BXQ-350 was well tolerated in both solid tumor and high-grade glioma (HGG) patients.

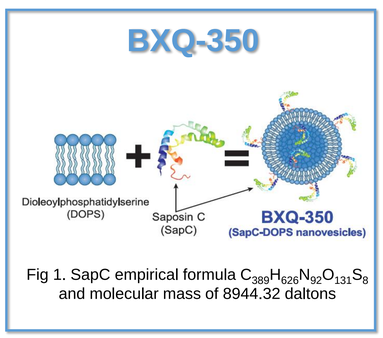

Fig 1. SapC empirical formula $C_{389}H_{626}N_{92}O_{131}S_8$ and molecular mass of 8944.32 daltons

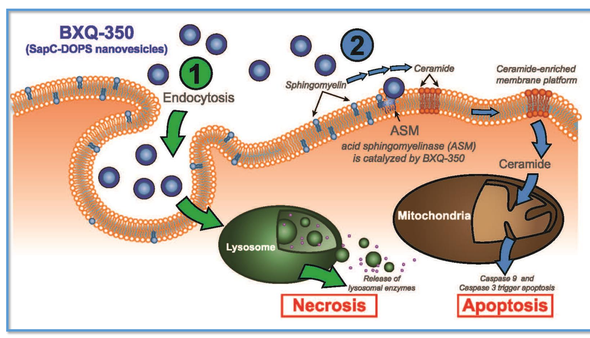

Fig 2. Illustration of BXQ-350 Mechanisms of Action
BXQ-350 nanovesicles bypass the blood-brain-barrier and selectively induce tumor cell death via lysosomal degradation (Wojton et al. 2013 *Mol Ther*; labeled mechanism #1 in green). It also acts by selectively inducing apoptosis via elevation of intracellular ceramides following caspase activation (Qi et al. *Clin Cancer Res 2009*; labeled mechanism #2 in blue).

METHODS

- A Phase 1a open-label, dose-escalation trial of BXQ-350 was conducted in refractory solid tumor and HGG patients. Escalating intravenous (IV) BXQ-350 doses of 0.7, 1.1, 1.4, 1.8, or 2.4 mg/kg were administered on Days 1-5, 8, 10, 12, 15, 22 (cycle 1) and every 28-days (subsequent cycles).
- A Phase 1b maximum tolerable dose study is ongoing, this poster will focus on outcomes of the HGG subset included in BXQ-350 Phase 1a and 1b with data available through 31 Aug 2018.
- Outcomes of 1a and 1b: MRI neuroimaging (e.g. Axial T1-post-contrast, Ax T2/FLAIR and medically necessary views) on Days 29, 57, 113, and 171 (or at withdrawal), RANO assessment, Neurological deficits, ECOG Performance Status, and Safety.

RESULTS

- The HGG patients in Phase 1a (9/17) were dosed at 0.7 (N = 1), 1.1 (N = 1), 1.4 (N = 2), 1.8 (N = 2), or 2.4 (N = 3) mg/kg, with 8/9 completing at least one full cycle before withdrawal (7 due to progression, 1 voluntary withdrawal). In Phase 1b, there are 7 HGG patients, 3 of which have received 1 cycle and 2 of which have received 2 cycles at 2.4 mg/kg.
- For Phase 1a patients with scores at baseline and progression (7/9), ECOG scores were stable at 0 or 1 from baseline to last measurement in 6/7 patients; 1 patient had a decline from 0 to 2. Phase 1b patients had stable scores, with the exception of one patient with baseline ECOG of 2 and decline to 3 and a second patient with baseline of 1 and gain of function to 0. (Table 2)
- BXQ-350 treatment was not associated with dose limiting toxicities or severe adverse reactions. (Table 2)
- One patient completing 6 cycles (>12 months) of BXQ-350 therapy (0.7 mg/kg) exhibited stable disease, -7% lesion size, and no significant progressive neurological deficits. Three patients underwent surgery while on treatment with two having disease progression and one reactive changes.

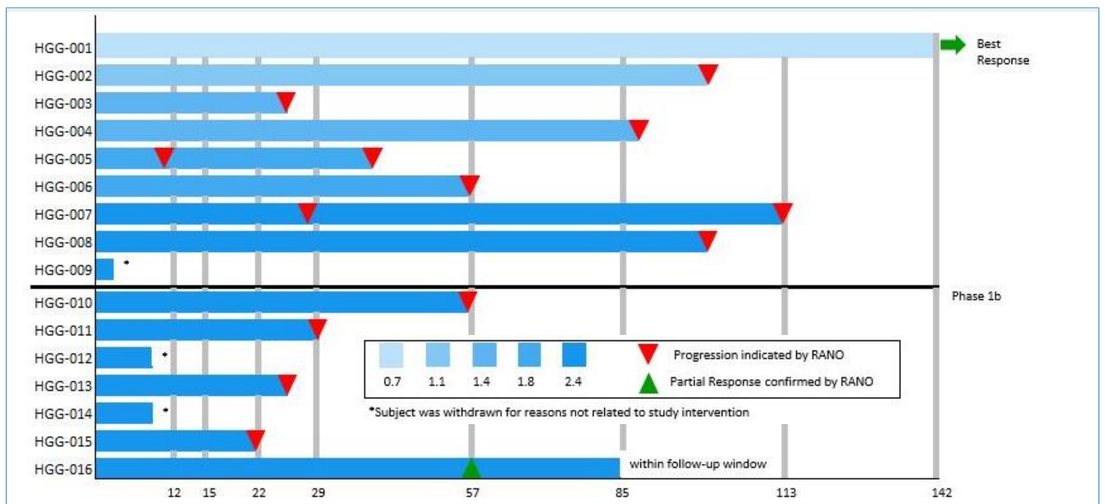

Figure 3. Swimmer plot of RANO outcomes in HGG

RESULTS

Table 1. HGG Patient Demographics by Dose Level

	Phase 1a					Phase 1b
	0.7 mg/kg N=1	1.1 mg/kg N=1	1.4 mg/kg N=2	1.8 mg/kg N=2	2.4 mg/kg N=3	2.4 mg/kg N=7
Age, mean (SD)	64.0	24.0	59.0 (1.4)	53.0 (0.0)	47.3 (18.2)	54.1 (15.28)
Gender, male n (%)	1 (100)	1 (100)	1 (50)	2 (100)	3 (100)	3 (42.9)
Race, white n (%)	1 (100)	1 (100)	2 (100)	2 (100)	3 (100)	6 (85.7)
Histology Grade						
III	-	-	-	-	-	1(14.3)
IV	1 (100)	1(100)	2 (100)	2 (100)	3 (100)	6 (85.7)

Table 2. HGG Patient ECOG and Safety by Dose Level

	Phase 1a					Phase 1b
	0.7 mg/kg N=1	1.1 mg/kg N=1	1.4 mg/kg N=2	1.8 mg/kg N=2	2.4 mg/kg N=3	2.4 mg/kg N=7
Number of cycles completed	6	4	1, 3	2, 2	0, 3, 4	0 (2 pts) 1 (3 pts) 2 (2 pts)
ECOG at baseline						
0	1	-	1	1	-	2[c]
1	-	1	1	-	3[b]	2
2	-	-	-	-	-	3
3	-	-	-	-	-	
ECOG at progression						
0	1	-	1	-	-	2
1	-	1	1	1[a]	2	1
2	-	-	-	1	-	2
3	-	-	-	-	-	1
Adverse Events (n cases, n events)						
Moderate severity, related	-	1, 2	1, 1	-	-	1, 2
Atelectasis	-	-	-	-	-	1, 1
Balance	-	1, 1	-	-	-	-
Dyspnoea	-	-	-	-	-	1, 1
Dysarthria	-	1, 1	-	-	-	-
Urinary tract Infection	-	-	1, 1	-	-	-
Serious, non-related	-	-	1, 2	-	1, 3	3, 6
Aphasia	-	-	1, 1	-	-	-
Delirium	-	-	-	-	-	1, 1
Diarrhea	-	-	-	-	1,1	-
Nausea	-	-	-	-	1,1	-
Vomiting	-	-	-	-	1,1	-
Fall	-	-	-	-	-	1, 1
Headache	-	-	-	-	-	1, 1
Hypernatraemia	-	-	-	-	-	1, 1
Muscular Weakness	-	-	1,1	-	-	-
Mental Status Change	-	-	-	-	-	1, 1
Radius Fracture	-	-	-	-	-	1, 1

a ECOG not measured at baseline, b ECOG not measured at progression, c ECOG not measured at progression

CONCLUSION

- BXQ-350 (SapC-DOPS) is a first-in-class nanoliposomal agent with a unique mechanism of action, which induces cytotoxicity through lysosomal degradation and ceramide-mediated apoptosis.
- In this Phase I study, BXQ-350 was well tolerated by HGG patients with promising radiological best response suggesting potential therapeutic benefit and warranting further trials.

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Learn more about our research at: