First-in-human, First-in-class Phase 1a Study of BXQ-350 for Solid Tumors and Gliomas

Olivier Rixe,1 John Charles Morris,3 Vinay K. Puduvalli,1 John L. Villano,3 Trisha M. Wise-Draper,2 Carolyn Muller,3 Angela N. Johnson,3 Robert Wesolowski,2 Xiaoyang Qi1

INTRODUCTION

BXQ-350 is a novel agent composed of the multifunctional lipid, sphingomyelinase activator protein Saposin C (SapC) and dihydroxo-oleoyl-phosphatidylserine (DOPS) tethered to a bisphosphonate conjugate. Biophysical studies and small animal models indicate that exposure to tumor cells tends to accumulate in diseased tissues due to insufficient clearance. BXQ-350 is thought to directly activate SapC, which cleaves endogenous sphingomyelin to ceramide and phosphatidylyserine, promoting autophagy and apoptosis.

METHODS & STUDY DESIGN

Study Design
A Phase 1a, open-label, dose-escalation trial of BXQ-350 (injections) was conducted in solid tumors and gliomas. BXQ-350 was administered by intravenous injection (IV) by administering escalating intravenous (IV) doses. BXQ-350 doses (1.1–1.4 mg/kg in mice and 0.25–2.0 mg/kg in humans) were determined to be too toxic for further evaluation. BXQ-350 was evaluated in 16 evaluable patients (9 solid tumors, 7 gliomas) and 10 evaluable days (13 evaluable days).

Target Enrollment
The study aimed to enroll 20 patients with solid tumors (N=67 assessed; Phase 1, 16). The primary aim of the Phase 1 portion of the study was to conduct experiments to define dose to begin Phase 2. Sequential cohorts of patients with susceptible solid tumors (ranging from 1-6) were treated with escalating doses of BXQ-350 until the maximum tolerated dose (MTD) was established in a high planned dose.

RESULTS

PK Results
The PK profile followed a predictable trend that was dose proportional with half-life and C max remaining constant (0.5-1.4 h and 0.07-5.09 ng/mL, respectively).

Safety Results
At least 1 of 27 patients (age 57) with a median (range) 2.1 (0.8-3.8) in patients treated with a median of 2.1 (0.8-3.8) for treatment-emergent adverse events (TEAEs). TEAEs included all patient experienced symptoms (70%). Clinical chemistry (e.g., ALT, AST, and GGT) and laboratory tests were normal. There was no evidence of hypersensitivity or serious adverse events related to study intervention. BXQ-350 also appeared promising for treatment of solid tumors, as evidenced by partial response to BXQ-350 (19% partial response rate).

RANO/RECIST Results
Best response in 1 patient completing study day 113 was partial response (progression-assessed at 2.3 mg/kg and 2.4 mg/kg). A 6.7 mg/kg dose was not reached at maximum planned dose.

Globally Enrolled Data
BXQ-350 was also well tolerated and without DLTs or treatment-related SAEs at the maximum planned dose. The PK profile followed a predictable trend that was dose proportional with half-life and C max remaining constant (0.5-1.4 h and 0.07-5.09 ng/mL, respectively).

CONCLUSIONS

In summary, the Phase 1a study showed that:
1. BXQ-350 was well tolerated with minimal or no treatment-related SAEs at the maximum planned dose.
2. The PK profile followed a predictable trend that was dose proportional with half-life and C max remaining constant (0.5-1.4 h and 0.07-5.09 ng/mL, respectively).
3. Preliminary activity was observed based on RANO/RECIST response in the study at 2.3 mg/kg.
4. These findings support the microenvironment-dependent nature of the drug and its potential for future clinical development.
5. Based on this data, the Phase 2 portion of the study is currently ongoing an estimated end date in early 2019.

REFERENCES


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