Clin Cancer Res. 2024 Sep 12. doi: 10.1158/1078-0432.CCR-24-1721. Online ahead of print.

A first-in-human phase 1 study of BXQ-350, a first-in-class sphingolipid metabolism regulator, in patients with advanced/recurrent solid tumors or high-grade gliomas

Olivier Rixe [1], John L Villano [2], Robert Wesolowski [3], Anne M Noonan [4], Vinay K Puduvalli [5], Trisha M Wise-Draper [6], Richard Curry [7], Emrullah Yilmaz [5], Charlie Cruze [8], Besim Ogretmen [9], Gilles Tapolsky [8], Ray Takigiku [8]

Affiliations

PMID: 39264252 DOI: 10.1158/1078-0432.CCR-24-1721

Abstract

Purpose: BXQ-350, a nanovesicle formulation of Saposin C, is an allosteric sphingolipid metabolism regulator that increases pro-apoptotic ceramide and decreases oncogenic sphingosine-1-phosphate (S1P) levels. We conducted a first-in-human, phase 1 study of BXQ-350.

Patients and methods: Adults (≥18 years old) with advanced/recurrent, treatment-refractory solid tumors or high-grade gliomas received BXQ-350 intravenously in five dose cohorts (0.7-2.4 mg/kg) in a 3+3 dose-escalation and expansion design. Primary endpoints during dose escalation were dose-limiting toxicities (DLTs) and maximum tolerated dose (MTD); primary objective in expansion parts was assessment of anti-tumor activity (RECIST v1.1/RANO criteria).

Results: Eighty-six patients were enrolled. DLTs were not observed during dose escalation (n=18), and a MTD was not identified. An additional 68 patients received the 2.4 mg/kg dose. Nine patients (10%) discontinued due to adverse events (AEs). The most common treatment-related AEs were nausea (24%) and fatigue (23%). Eight patients had a progression-free survival (PFS) ≥6 months. Two of these achieved a partial response, and six had stable disease, among whom three had a reduction in ≥1 target lesion. Of those with PFS ≥6 months, seven remained on study for >12 months, five for >24 months, and after seven years, two remained on study without disease progression.

Conclusions: BXQ-350 was well tolerated as monotherapy at doses up to 2.4 mg/kg. It provided some lasting clinical benefit in patients with recurrent solid malignancies across several tumor types, consistent with a decreased systemic S1P/ceramide metabolic rheostat. BXQ-350 warrants further clinical investigation alone and combined with standard-of-care for advanced solid tumors.