Background Patients with locally advanced or metastatic cancer have poor prognosis despite treatment advancements. VSV-GP (BI 1831169) is a chimeric vesicular stomatitis virus (VSV) with its neurotropic glycoprotein (G) replaced by the non-neurotropic glycoprotein (GP) of the lymphocytic choriomeningitis virus. This live, recombinant oncolytic virus has demonstrated preclinical efficacy as a viral-based immunotherapy due to its interferon-dependent tumor specificity and stimulation of antitumor immune activity. Co-administration of ezabenlimab (BI 754091), a PD-1 targeting checkpoint inhibitor, may enhance antitumor efficacy. The potential synergism of VSV-GP and ezabenlimab will be explored in this first-in-human trial.

Methods This Phase I, open-label, dose-escalation trial will assess the safety, tolerability and early efficacy of VSV-GP given intratumorally (IT), intravenously (IV) or both, as a monotherapy (Part 1) and in combination with ezabenlimab (Part 2) in patients with locally advanced, metastatic or relapsed/refractory solid tumors who previously received or are not candidates for available standard treatment. Key objectives are to determine the maximum tolerated dose (MTD) and recommended Phase 2 dose (RP2D).

Part 1 is a dose-escalation and expansion study of VSV-GP monotherapy administered in four 21-day cycles starting at $5 \times 10^7$ median tissue culture infectious dose (TCID$_{50}$) in Arm A (IT) and at the next tolerated dose level in Arm B (IV) and Arm C (IT + IV). Part 2 is a dose-escalation study of VSV-GP in combination with ezabenlimab. The starting dose of VSV-GP will be one dose level less than the monotherapy RP2D in the corresponding Part 1 arm (IT [Arm D], IV [Arm E], IT + IV [Arm F]) (figure 1). Dose finding will be guided by the Bayesian Optimal Interval design (BOIN).

Primary endpoints include the number of patients experiencing dose-limiting toxicities (DLTs [Part 1/2]) and objective response according to Intratumoral RECIST$^\text{I}$ (itRECIST; Part 1). Secondary endpoints are safety-based (on-treatment DLTs and adverse events). Patients are being recruited. Updates will be provided at the time of presentation.$^1$

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REFERENCE