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 anti-tumor 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 (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.

Acknowledgements The authors meet criteria for authorship as recommended by the International Committee of Medical Journal Editors (ICMJE). The authors did not receive payment related to the development of the abstract. Devon Else, BSc, of MediTech Media provided writing and editorial support which was contracted and funded by Boehringer Ingelheim International GmbH (BI). BI was given the opportunity to review the abstract for medical and scientific accuracy as well as intellectual property considerations. The 1456.1 study was supported and funded by BI.

Trial Registration NCT05155332

REFERENCE