AN OPEN-LABEL PHASE I DOSE-ESCALATION CLINICAL TRIAL TO EVALUATE THE SAFETY, TOLERABILITY, PHARMACOKINETIC PROFILE AND PRELIMINARY EFFICACY OF VG161 IN PATIENTS WITH ADVANCED PRIMARY LIVER CANCER

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Background VG161 is a novel HSV-1 oncolytic virus expressing IL-12, IL-15, IL-15 receptor alpha subunit isoform 1 (IL-15Ra), and a PD-1/PD-L1 blocking peptide (TF-Fc). This is to report the preliminary clinical and translational data from 11 efficacy evaluable patients.

Methods In this multicenter phase I trial, we enrolled 11 patients with advanced primary liver cancer refractory to standard therapy including immune checkpoint inhibitor (ICI). VG161 was administrated by imaging guided intra-tumoral injection. Based on preclinical NOAEL, the initial dose level was 1×10^8 PFU/subject, followed with 4 cohorts (1×10^8, QD for D1 and D2; 1×10^8, QD for D1-3; 1.3×10^8, QD for D1-3; and 1.7×10^8, QD for D1-3). Fast titration design was used for the first 2 cohorts and followed by standard 3 + 3 design. For PK and viral shedding, virus DNA was measured in blood, urine, oral and injection site swabs by a validated PCR test. Changes of cytokines and lymphocyte subsets in blood was also measured. Antitumor activity was assessed by RECIST1.1 and iRECIST. Overall survival (OS) was recorded.

Results Eleven patients (aged from 43-74, 9 males and 2 females; 8 HCC and 3 ICC) were enrolled between April 2021 and January 2022. By 10 May 2022, all patients had at least one tumor assessment. No dose limiting toxicity (DLT) was observed. The most common treatment related adverse event (TRA) was fever (100%). No dose limiting toxicity (DLT) was observed. One serious adverse events (SAEs), Grade 2 sub-facial paralysis (33.3%) was seen in 1 patient, which is related to study drug, no immune-related adverse events (irSAEs) occurred. One ICC patient in 3rd cohort (9%) had immune partial response (iPR) with PFS of 5.3 month based on both iRECIST and RECIST 1.1. Another 2 patients with HCC in the 1st and 2nd cohort had prolonged PFS of 3.7 and 11.5 months respectively. The levels of each T cell immune-related parameter including PD-L1, PD-1, CD69 and CD8+Ki67^high of subjects in each cohort showed an increasing trend after VG161 administration. To date, the median follow-up time is 7.8(2.3-15.6), significantly prolonged OS was seen in 5 patients received ICI after the trial (p=0.025).

Conclusions Image guided IT injection of VG161 up to 3 times of 1.7×10^8 PFU/subject was safe and well tolerated, with no unexpected viral spread or shedding. The efficacy of prolonged PFS in 3 patients and PR in 1 patient is encouraging and needs to be further investigated. Clinical trial information: NCT04806464.

Trial Registration NCT04806464

Ethics Approval The study was approved by the Ethics Committee of the First Affiliated Hospital, School of Medicine, Zhejiang University, approval number 20191101.

Consent Written informed consent was obtained from the patient for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.