1532 A PHASE 1/2 STUDY OF SAFETY, TOLERABILITY, AND PHARMACOKINETICS OF SNS-101, A PH-SENSITIVE ANTI-VISTA MAB, AS MONOTHERAPY AND IN COMBINATION WITH CEMIPLIMAB IN PATIENTS WITH ADVANCED SOLID TUMORS

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Background VISTA (V-domain Ig suppressor of T-cell activation) is a significant emerging immuno-oncology target. Despite the therapeutic potential of VISTA inhibition demonstrated in preclinical studies,[1] clinical development of anti-VISTA antibodies has been challenging due to dose-limiting on-target cytokine release at sub-therapeutic doses and target mediated drug disposition (TMDD).[2] SNS-101 is a fully human IgG1 monoclonal antibody designed to selectively disrupt the VISTA:PSGL-1 immune checkpoint in the acidic tumor microenvironment. Preclinical data demonstrate the potential of SNS-101 to exhibit favorable safety and tolerability profiles and promote anti-tumor activity as monotherapy or in combination with PD-1 blockade.[3–5]

Methods This is a first-in-human, open-label, multi-center, dose escalation and expansion study to evaluate the safety, tolerability, pharmacokinetics (PK), pharmacodynamics and efficacy of SNS-101 as monotherapy or in combination with cemiplimab in patients with advanced solid tumors (NCT05864144). The study is being conducted in 3 parts: Part A: Phase 1 (P1) Monotherapy Dose Escalation (SNS-101 alone); Part B: P1 Combination Dose Escalation (SNS-101 + cemiplimab); Part C: Phase 2 (P2) Expansion Cohorts (SNS-101 ± cemiplimab). Patients will receive SNS-101 ± cemiplimab as intravenous infusion(s) every 3 weeks and may continue until confirmed progressive disease or unacceptable toxicity. Dose escalation follows the Bayesian Optimal Interval Design until the Maximum Tolerated Dose (MTD)/Recommended Phase 2 Dose (RP2D) is determined. Primary objectives include safety, tolerability and RP2D/MTD (P1), and evaluation of anti-tumor activity (P2). Safety and tolerability assessments include monitoring of dose limiting toxicities (DLTs) and adverse events (AEs), PK, anti-drug antibodies and inflammatory cytokine release. Tumor imaging and T-cell immunophenotyping are being utilized to monitor responses.

Results As of August 31, 2023, 7 patients were enrolled in Part A across three dosing cohorts (0.3 mg/kg, 1 mg/kg and 3 mg/kg). No DLTs or CRS events were noted. Nine AEs (8/9 Grade 1–2) have been reported in 5 patients. One Grade 5 AE related to disease progression and not to the treatment was observed. One AE, dermatitis acneiform, is considered treatment-related. Infusions have not required premedications. PK results show high concordance with preclinical modeling data, demonstrating dose-proportional exposure, linear elimination kinetics, and suggesting the absence of TMDD.

Conclusions SNS-101 has been well tolerated and effectively dosed ≥ 10-fold higher than first-generation VISTA targeting antibodies. Preliminary clinical data support our hypothesis that pH-sensitive targeting of VISTA with SNS-101 may overcome safety and tolerability challenges encountered with non-pH-selective anti-VISTA antibodies. Updated data from ongoing cohorts will be presented.

Trial Registration NCT05864144 (Start May 2023, Est. Close June 2027)

ClinicalTrials.gov, Trial #NCT02671955.

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Ethics Approval This study was conducted in accordance with the Declaration of Helsinki ethical principles, guidelines for Good Clinical Practice, and requirements of public registration of clinical trials. The protocol, the informed consent form and other written materials provided to participants, and any other relevant study documentation was approved by the Institutional Review Board associated with each clinical site with enrolled patients. Written informed Consent was obtained from each subject at enrollment.

http://dx.doi.org/10.1136/jitc-2023-SITC2023.1532