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A Phase 1 Trial of the Oncolytic Virus SVV-001 with Nivolumab and Ipilimumab in Patients with High Grade Neuroendocrine Neoplasms.

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BACKGROUND

High-grade neuroendocrine neoplasms (NENs) are aggressive malignancies with limited treatment options. Immune checkpoint inhibitors (ICIs) have demonstrated meaningful but limited efficacy. Seneca Valley Virus (SVV-001) is a novel oncolytic RNA virus that has shown synergistic antitumor activity with ICIs in preclinical models. Additionally, SVV-001 has shown a favorable safety profile and the ability to reverse ICI resistance in vivo, supporting its evaluation in combination with nivolumab + ipilimumab (N+I).

METHODS

NCT06889493 is an investigator-initiated, phase 1 study evaluating intratumoral SVV-001 with N+I in patients with high-grade NENs. A 3+3 dose-escalation design will determine the recommended phase 2 dose (RP2D) with 3 single-injection dose levels (DL1-3) and 2 multiple-injection DLs (4-5), followed by expansion at the RP2D. The primary objective is to evaluate safety with secondary objectives being efficacy. Tumor Endothelial Marker 8 (TEM8), a potential biomarker of SVV-001 sensitivity and its association with efficacy signals will be investigated.

RESULTS

As of 1st July 2026, the trial has reached the end of the single-dose injection milestone with 13 pts (pts) enrolled on DLs 1-3. No DLTs were observed to date. Seven pts (54%) experienced Grade 3 serious adverse events (SAEs) unrelated to SVV-001 [abdominal pain (n=2); pneumonia, intracranial hemorrhage, anorexia, fatigue, biliary obstruction, seizure, fever (n=1)]. Other grade 3 AEs were observed in five (38%) pts; most common were anorexia (n=3), alanine aminotransferase increased and fatigue (n=2). Two

pts (15%) achieved a partial response, 2 (15%) had stable disease, 6 (46%) came off study due to disease progression, and 3 (23%) are currently receiving treatment– the objective response rate was 15% and the disease control rate was 31%. Biomarker analysis is ongoing. The multiple-dose injection DLs will begin enrollment in July 2026.

CONCLUSIONS

Single-dose injection of SVV1 with N+I demonstrates an acceptable safety profile and early signs of efficacy in a disease of a significant unmet need.

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