Phase I Trial of Seneca Valley Virus (NTX-010), a Newly Discovered Systemically Deliverable Oncolytic Picornavirus, in Patients with Solid Tumors with Neuroendocrine Features

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ABSTRACT

Background: SVV-010 is a naturally occurring wild type picornavirus which is highly selective to human neuroendocrine tumor cells.

Methods: This phase I trial used escalating dose cohorts of NTX-010 in patients with small cell lung cancer, other neuroendocrine tumors, and other advanced solid tumors. Safety, viral kinetics, and antitumor activity were assessed in 41 patients treated in cohorts of 1-5 patients.

Results: Early toxicities were noted at dose level 1 and included flu-like symptoms, cytokine release syndrome, and viral shedding. No additional toxicity was observed at subsequent dose levels. SVV-010 demonstrated antitumor activity in patients with small cell lung cancer including improvement in carcinoid syndrome symptoms, decline in 5HIAA and other serum markers, minor responses by CT scan, and durable responses following single IV dosing in multiple xenograft models.

Conclusions: The NTX-010 clinical trial is ongoing, and receipt of a biologic license or a clinical development license is anticipated in the near future.

METHODS

Eligibility: Two primary cohorts of patients have been studied to date: a dose escalation cohort in patients with any NET cancer with estimated survival ≤ 6 months, and an expansion cohort of advanced SCLC treated at 10^3 vp/kg.

ASSESSMENTS

• Chromoparin A
• Viral replication assessment in serum, stool, urine and sputum
• Regular repeat imaging (CT/MR/PET) on a 6-8 week basis
• Pre and post therapy antibody assays for neutralizing antibodies

RESULTS

Small Cell Cohort: safety and efficacy
- Small cell patients in this study had progressive disease following multiple lines of therapy. Typically 2–5 lines
- All small cell patients were dosed at the lowest dose level (10^5 VP/KG)
- One of the 6 patients in this cohort has experienced long term survival of more than 18 months, and has returned to work.
- Limited historical data is available on expected PFS and OS beyond third line therapy for small cell.
- Overall Survival KM (as of 1/4/09)

CONCLUSIONS

- No DLT’s at any dose
- Primary AE: Mild flu like symptoms for 1-2 days
- No apparent correlation between viral replication and adverse events
- Clinical effects apparent from safety study
  - Small Cell Lung Cancer: Long term survival in 1 of 5 subjects
  - Positive survival trend supports further development
- Phase II study in SCLC planned with a cooperative group during the watchful waiting period. Trial to start in 2009