

## ADVL0911: A Phase 1 Dose Escalation Study of Seneca Valley Virus (NTX-010), A Replication-Competent Picornavirus, in Relapsed/Refractory Pediatric Patients With Neuroblastoma, Rhabdomyosarcoma, or Rare Tumors With Neuroendocrine Features

Type	Status	Age Range (yrs.)	Sponsor
Interventional	Open Label	3 to 21 years	CCHMC

### Purpose

This phase I trial is studying the side effects and best dose of Seneca Valley virus-001 in treating young patients with relapsed or refractory neuroblastoma, rhabdomyosarcoma, or rare tumors with neuroendocrine features.

### Rationale

Seneca Valley virus-001 may be able to kill certain kinds of tumor cells without damaging normal cells.

### Objectives

#### Primary

- To estimate the maximum tolerated dose and/or recommended phase II dose of Seneca Valley virus-001 (NTX-010) when administered as a single infusion to pediatric patients with relapsed or refractory neuroblastoma, rhabdomyosarcoma, or rare tumors with neuroendocrine features (Wilms tumor, retinoblastoma, adrenocortical carcinoma, or carcinoid tumors).
- To confirm that there is viral replication in these patients following NTX-010 administration.
- To define and describe the toxicities of NTX-010 when administered on this schedule.
- To characterize the pharmacokinetics (time course of viral clearance) following NTX-010 administration in these patients.

#### Secondary

- To preliminarily define the antitumor activity of NTX-010 within the confines of a phase I study.
- To evaluate the development of neutralizing antibodies to NTX-010 following IV administration of NTX-010.
- To investigate the presence and permissivity of occult circulating tumor cells prior to and after intravenous administration of NTX-010.

### Outline

This is a multicenter study.

Patients receive Seneca Valley virus-001 (NTX-010) IV over 1 hour on day 1.

Tumor tissue samples are collected at baseline for biomarker studies. Blood and stool samples are collected periodically for neutralizing antibody and viral clearance studies.

After completion of study treatment, patients are followed up periodically for up to 1 year.

## Eligibility

Ages eligible for study: 3 to 21 years

## Disease Characteristics:

- Histologically confirmed diagnosis of 1 of the following:
  - Neuroblastoma
  - Rhabdomyosarcoma
  - Wilms tumor
  - Retinoblastoma
  - Adrenocortical carcinoma
  - Carcinoid tumor
- Relapsed or refractory disease
- Measurable or evaluable disease
- No known curative therapy or therapy proven to prolong survival with an acceptable quality of life
- No known pulmonary tumors or metastases > 5 cm, as evaluated by chest CT scan
- No clinically significant pulmonary and/or pericardial effusions ( $\leq$  grade 3), as evaluated by ECHO
- No primary CNS tumors or known metastatic CNS disease involvement

## Patient Characteristics

- Karnofsky performance status (PS) 50-100% (for patients > 16 years of age)
- Lansky PS 50-100% (for patients  $\leq$  16 years of age)
- Peripheral ANC  $\geq$  1,000/mm<sup>3</sup>
- Platelet count  $\geq$  100,000/mm<sup>3</sup> (transfusion independent, defined as no platelet transfusions within a 7-day period before study enrollment)
- Hemoglobin  $\geq$  8.0 g/dL (RBC transfusions allowed)
- Creatine clearance or radioisotope GFR  $\geq$  70 mL/min/1.73m<sup>2</sup> OR serum creatinine based on age/gender as follows:
  - $\leq$  0.8 mg/dL (for patients 3 to 5 years of age)
  - $\leq$  1.0 mg/dL (for patients 6 to 9 years of age)
  - $\leq$  1.2 mg/dL (for patients 10 to 12 years of age)
  - $\leq$  1.4 mg/dL (for female patients  $\geq$  13 years of age)
  - $\leq$  1.5 mg/dL (for male patients 13 to 15 years of age)
  - $\leq$  1.7 mg/dL (for male patients  $\geq$  16 years of age)
- Bilirubin (sum of conjugated and unconjugated)  $\leq$  1.5 times upper limit of normal (ULN)
- SGPT  $\leq$  110 U/L (for the purpose of this study, the ULN for SGPT is 45 U/L)
- Serum albumin  $\geq$  2 g/dL
- Oxygen saturation > 92% on room air

- Not pregnant or nursing
- Negative pregnancy test
- Fertile patients must use effective contraception
- Able to comply with the safety monitoring requirements of the study, in the opinion of the investigator
- Completely toilet trained
- No chronic diarrhea or urinary incontinence during the day or night, and no in-dwelling urinary catheters
- No uncontrolled infection
- No known pregnant member of the household

### Prior Concurrent Therapy

- Fully recovered from the acute toxic effects of all prior chemotherapy, immunotherapy, or radiotherapy
- At least 6 months since prior total-body irradiation (TBI), craniospinal radiotherapy, or radiotherapy to  $\geq 50\%$  of the pelvis
- At least 3 months since prior stem cell transplantation or rescue (without TBI)
  - No evidence of active graft-vs-host disease
  
- At least 6 weeks since other prior substantial bone marrow radiotherapy or treatment with therapeutic doses of MIBG
- More than 3 weeks since prior myelosuppressive chemotherapy
- At least 2 weeks since prior local palliative radiotherapy (small port)
- More than 7 days since prior growth factor(s) that support platelet or white blood cell number or function
- At least 7 days since prior biologic agents
- At least 3 half-lives since prior monoclonal antibodies
- More than 7 days since prior viral immunizations, including influenza
- No other viral immunizations during or for 28 days after Seneca Valley virus-001 infusion
- Concurrent corticosteroids allowed provided the patient has been on a stable or decreasing dose for the past 7 days
- No other concurrent investigational drugs or anticancer agents (e.g., chemotherapy, radiotherapy, immunotherapy, or biologic therapy)

### For More Information Contact:

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