CALM study: A Phase II study of intratumoral Coxackievirus A21 in patients with stage IIIc and stage IV malignant melanoma


Huntsman Cancer Institute, University of Utah, Salt Lake City, UT; Rush University Medical Center, Chicago, IL; UCSF Moores Cancer Center, La Jolla, CA; Northern California Melanoma Center, San Francisco, CA; Mount Sinai Comprehensive Cancer Center, Miami Beach, FL; Oncology Specialists SC, Niles, IL; Atlantic Melanoma Center, Morristown, NJ; Mary Crowley Cancer Research Center, Dallas, TX; Pharmaceutics3, Princeton, NJ; Investigative Clinical Research of Indiana, IN; Viralytics, Sydney, Australia; Viralytics Limited, Sydney, Australia

**Introduction**

Coxackievirus A21 (CVA21: CAVATAK™, CVA21) is a naturally occurring replication competent virus; it causes mild upper respiratory illness "common cold"; Coxsackievirus A21 (CVA21) is a naturally occurring enterovirus C genus of the family Picornaviridae; Coxsackievirus A21 binds to the N-terminal domain of intercellular adhesion molecule-1 (ICAM-1); Coxsackievirus A21 can bind multiple ICAM-1 molecules; targets cancer cells expressing high surface levels of ICAM-1; numerous different types of cancer cells express high levels of ICAM-1.

**Objectives**

**Primary Objective:**
- To assess the clinical efficacy of intratumoral (IT) CVA21 in terms of Progression-Free Survival (irPFS) at 6 months as monitored via immune-related Response Criteria (irRC) (immune-related RECIST 1.1).

**Secondary Objectives:**
- To assess the clinical efficacy of IT CVA21 in terms of Durable Response Rate (DRR) at 6 months.
- To assess the clinical efficacy of IT CVA21 in terms of DFS as monitored via RECIST1.1, 1-year survival and Overall Survival (OS).
- To assess the clinical efficacy of IT CVA21 in terms of Disease Control Rate (i.e., Complete Response [CR] + Partial Response [PR] + Stable Disease [SD]) as monitored via irRC (immune-related RECIST 1.1) at 6 months, i.e., immunediated Disease Control Rate (iDCR) at 6 months.
- To assess the safety of IT CVA21 in terms of adverse events, viral biodistribution, and serum antibody response to CVA21.

**Methods**

The CALM study investigates the efficacy and safety of intratumoral CVA21 in approximately 63 pts with treated or untreated inoperable Stage IIIc-IVM1c melanoma. Pts are treated with up to 3 x 10^9 TCID50 intratumorally on study days 1, 3, 6, and 21 then every three weeks for an additional 6 injection. Key eligibility criteria are ≥ 18 yrs old, ECOG 0-1, and at least 1 intractable cutaneous, oc, or nodal tumor >1.0cm. The primary endpoint is irPFS at 6 months following to secondary endpoints include durable response rate and OS. A 2-stage Simon's minimax design will be employed. Based on data from previous trials and literature, a target overall irPFS at 6 months of 22.5% versus 10% (the null hypothesis) will be assessed using Fisher's test. With an alpha level of 1 and power of 80%, a total of 54 evaluable patients will be required to test the null hypothesis that the true irPFS rate is ≥10% versus the alternative hypothesis that the true irPFS rate is ≤10%.

**Results**

Currently, 35 patients have been enrolled on the study and treated with CVA21 injections. No grade 3 or 4 AE or SAE toxicities have been observed related to the study medication. Overall, the treatment has been well tolerated. The Stage I interim efficacy endpoint of 3 objective responses has been achieved, and the second stage of the study is proceeding with a planned enrollment of a total of 63 patients.