



CZ BIOMED CORP

Headquarters: 2203 N Lois Ave 9th Floor, Tampa FL 33607

Phone: 813-600-4088 **Fax:** 813-830-6112

RONALD E. WHEELER, M.D. MEDICAL DIRECTOR

IN CHARGE OF PROSTATE CANCER CLINICAL STUDIES WORLDWIDE

Prostate Cancer Vaccine Oncolytic Virotherapy

Oncolytic virotherapy is a novel strategy using viruses, either naturally occurring or genetically modified, to selectively target and destroy tumor cells while leaving surrounding non-malignant cells unharmed. The destruction of cancer cells occurs either through direct lytic rupture by multi-cycle viral replication or the subsequent induction of apoptosis and successful application of virotherapy requires preferential and efficient amplification of the virus to kill cancer cells. **PRORVLYSIN®** is a new class of potent genetically engineered common cold-like virus that selectively kills prostate cancer cells, but not normal healthy cells. With this medical breakthrough will potentially help millions of people worldwide in the fight against prostate cancers. Thus, **PRORVLYSIN®** is vastly safer to use and easier to process, as compared to traditional chemo- or radio-therapies of tumors, allowing patients to enjoy a much higher quality of life during treatment.

Side Effects of Prostate Cancer Vaccine Oncolytic Virotherapy

PRORVLYSIN® therapy may cause common cold-like symptoms such as chills, fever, muscle aches, headache, and weakness, loss of appetite, nausea, vomiting, or diarrhea. Patients may also experience other side effects including the tendency to bleed or bruise easily, and some get a rash. Home treatment to ease symptoms and prevent complications is usually all that is needed. Some of these problems may be severe, but they go away after the treatment stops.

Protocol: prostate cancer Vaccine treatment using oncolytic Virotherapy PRORVLYSIN® (Final Version)

Purpose

Rationale: A gene-modified virus may be able to kill prostate cancer cells without damaging normal cells.

Purpose: This phase I/II trial is studying the side effects and best dose of oncolytic virus therapy in treating patients with progressive, recurrent, or refractory prostate cancer or the patients with early stage of cancer.

Inclusion and exclusion criteria

Estimated enrollment: ≥20

Intervention details:

Biological: an engineered oncolytic virus---PRORVLYSIN®

Patients:

First week:

- (1) Harvest serum from patient for viral antibody test (Pre-Treatment)
- (2) Locally receive IV 1×10^{10} pfu/ml of PRORVLYSIN® (3 ml for intratumor and 10 ml for IV) on Friday, and receive IV 1×10^{10} pfu/ml at the following two days (Saturday and Sunday)
- (3) Harvest serum, urine and saliva at day 8 to test virus.

Second week (day 15~):

- (1) Receive IV 1×10^{10} pfu/ml of PRORVLYSIN® /day on Friday, Saturday and Sunday;
- (2) Harvest serum from treated patients at day 15 for antibody testing.

Fourth week (day 29~):

Receive IV 1×10^{10} pfu/ml of PRORVLYSIN® /day on Friday, Saturday and Sunday.

Inclusion Criteria:

- Evidence of progressive disease in the above categories evaluated by standard tumor staging.
- Histologically confirmed diagnosis or 3.0 T MRI confirmed.
- Failure of conventional anti- cancer modalities. Despite optimal application of all relevant available anti- cancer modalities.
- Age between 20 and 90 years old.
- Life expectancy \geq 12 months.
- ECOG performance status 0-2.(Ambulatory)
- Gleason Score (\geq 6) or MRI (+) for Prostate Cancer.
- Absolute neutrophil count \geq 1,500/mm³.
- Platelet count \geq 100,000/mm³. Perform PT, PTT and Platelets
- Liver Panel: AST and ALT with a normal bilirubin being ideal associated with an AST \leq 2 times the upper limit of normal ULN.
- Creatinine \leq 1.5 ULN. Perform Creatinine and BUN
- Hemoglobin \geq 9.0 g/dL.
- No active infection within the past 5 days.
- No active heart disease.
- No requirement for blood product support.
- No seizure disorders.
- No history of immunodeficiency.
- No history of asthma.
- A written informed consent understood and signed by the patient and witnessed by a spouse or significant other.

Exclusion Criteria:

- Not fulfilling any of the above criteria
- Moribund patients or patients with life- expectancy < 3 months
- ECOG performance status 3-4 (Non-Ambulatory)
- Active local or systemic infections requiring treatment
- History of asthma.
- Co-morbidity or life- threatening clinical condition other than the basic cancer.
- Inability to fly.

Primary Outcome Measures:

- Number of toxicity incidents
- Maximum tolerated dose (NCI Common Terminology Criteria version 4.0 will be used for grading the severity of AE. Dose Limiting Toxicity (DLT) will be defined as a study-related grade 3 or 4 AE).

Secondary Outcome Measures:

- PSA levels
- Tumor size (MRI confirmed changes; Pre versus Post Treatment)
- Time to progression
- Laboratory correlates

Detailed Description:

- Determine the safety and toxicity of PRORVLYSIN® in patients with progressive, recurrent, or refractory prostate cancer or the patients with early stage of tumor.
- Determine the maximum tolerated dose of PRORVLYSIN® in these patients.
- Characterize viral replication at each dose level as manifested by viral titers in these patients.
- Assess viremia, viral replication, and oncolytic virus shedding or persistence after study therapy.
- Determine humoral immune response to the injected virus in these patients.
- Assess, preliminarily, the antitumor efficacy of this therapy, by assessing PSA levels, tumor size, and time to progression, in these patients.

Blood, urine, and saliva samples will be collected at various time intervals, stored at -80°C, and later evaluated for viral recovery and host responses to viral therapy.

Research Facility at The University of South Florida Research Park

3802 Spectrum Blvd. Tampa, FL 33612

www.czbiomed.com