NIRPA

An Investigator Sponsored Retrospective/Prospective Study of a New Immunotherapy Regimen (MyVaccx™) for Patients with Adenocarcinoma

Protocol Number: NIRPA #1

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Study Sponsor:

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Through the practice of medicine, using FDA cleared or approved devices, methods and medication in a unique off-label manner, Dr. Gary Onik has treated twenty-four patients with the MyVaccx™ System for Adenocarcinoma in the following types of cancer:

- Prostate cancer (19 patients)
- Lung cancer (1 patient)
- Pancreatic cancer (1 patient)
- Colorectal cancer (1 patient)
- Bladder cancer (1 patient)
- Unknown primary cancer (1 patient)

This is a retrospective/prospective study to document the pertinent patient medical history, treatment performed and outcome using standardized Case Report Forms (CRF's) for those patients who meet the selection criteria. The information generated by the data included in the First Treatment and Second Treatment CRF's will be summarized in a White Paper authored by Dr. Gary Onik.

The patients who met the subject selection criteria will be prospectively monitored through their normal standard of care for their original cancer, which will be documented on the Follow-up CRF. Individual Follow-up CRFs will be generated for each follow-up event. The data collected will be used to update the White Paper on a periodic basis.

The subjects will not incur any additional costs above their routine follow-up for their original cancer and will not receive any additional experimental procedures.

BACKGROUND

MyVaccx™ cancer therapy enables the patient's immune system to fight off cancer by amplifying the abscopal effect. The Abscopal Effect is a phenomenon in the treatment of metastatic cancer where localized treatment of a tumor causes not only a shrinking of the treated tumor, but also a shrinking of tumors outside the scope of the localized treatment. R.H. Mole proposed the term "Abscopal" in 1953 to refer to effect of ionizing radiation "at a distance from the irradiated volume but within the same organism."

The MyVaccx Cancer Therapy is initiated by: Proprietary focal tumor "priming" with antigen presentation (medical device system) immediately followed by the intra-tumoral injection of a proprietary depot formulation containing multiple FDA approved checkpoint inhibitors and an FDA approved cytokine, fostering the creation of an autologous vaccine that impacts the cancer systemically. The patient is then receives daily systemic injections for two months of the cytokine to boost the immune system's ability to ramp up to address the large metastatic tumor burden. My Vaccx consists of up to two applications of the therapy, the initial and a

second "booster" that are 6-8 weeks apart (if required and the subject has agreed to a second "booster").

The rationale for treating patients with the MyVaccx system is because the patients have run through and out of alternative therapy options, so My Vaccx provides a new therapy option for very late stage disease where none currently exists.

The active drugs used in the depot formulation are a PD-1 (either OpDivo, or Keytruda) and CTLA-4 (Yervoy) checkpoint inhibitors, plus a sagramostim (Leukine), a GM-CSF cytokine. The checkpoint inhibitors are used to mitigate the tumor's ability to locally shut down the immune system, even after the tumor has been primed with antigens having been presented, and the GM-CSF cytokine is utilized to "ramp up" the local immune response to the tumor antigens once they have been recognized. The depot formulation also includes iodinated omnipaque contrast media, and ultrasound contrast media (perflutren – Definity) to aid in insuring that the intra-tumoral injection of the depot is optimally positioned. Post procedural medication includes Leukine daily for two months, which aids the immune system to handle the tumor burden on a systemic level.

Animal Study

There has been one (1) animal study conducted using the ablation modality which is part of the MyVaccx procedure. This study was published in the Journal of Clinical & Experimental Pathology, the abstract follows.[1]

Abstract: Electrical membrane breakdown (EMB) is a novel form of non-thermal treatment that has not, to our knowledge, been previously evaluated for its potential utility as an ablation mechanism. The findings with EMB immediately after treatment were compared with other forms of ablation (cryoablation and IRE (irreversible electroporation)) in the porcine liver clinically, ultrasonographically, and by light microscopy and ultrastructural analysis. Clinically, EMB did not induce muscular contractions, in contrast with IRE. By ultrasound, all lesions were hypoechoic when compared to the untreated liver. EMB created a consistent pattern of immediate tissue destruction at the light microscopic and ultrastructural level, characterized by pulse-dose-related coagulative necrosis and nuclear pyknosis, preserved blood vessels and adjacent structures, and sharply demarcated margins. We conclude that the profile of EMB ablation is distinctive and unique, inducing necrosis by immediate electrical rupture of cell membranes non-thermally while preserving proteins and adjacent vessels with potentially superior stimulation of the immune system than other ablation modalities

OBJECTIVES

The purpose of the proposed research study is to (1) document the findings of the patients which were treated with the MyVaccx™ System who meet the subject selection criteria and (2) prospectively monitor the treatment and longer-term outcome for these patients. The

information obtained from this research study will be used in the development process for a commercially viable MyVaccx™ System.

SUBJECT SELECTION

Subjects are included if they were treated with the MyVaccx™ System and are greater than 18 years of age. Two subjects with known visceral disease are being excluded based on the standard of other immunologic prostate cancer studies. Therefore, this study will include a maximum of twenty-two patients (total number to be defined based on subjects who sign the Informed Consent) out of the twenty-four treated with the MyVaccx™ System.

STUDY PROCEDURES

Informed consent from either the subject or their legal guardian will occur within approximately a one (1) month time-frame after receiving IRB approval to conduct the study. The Clinical research staff who have been trained on Good Clinical Practices by a CITI certified Clinical Research Associate will obtain signature of the informed consent of the subject or the subject's legally authorized representative by facsimile or e-mail. The consent interview will be conducted by telephone when the subject or subject's legally authorized representative has read the consent form during the discussion. After the consent discussion, the subject or the subject's legally authorized representative will sign and date the consent form and return the document by facsimile scanning and returning it through a secure e-mail account, or by posting it to a secure internet address. Alternatively, the subject may bring the signed and dated consent form to his/her next visit to the clinical site or mail it to the clinical investigator. The signed document will be filed with the subject's case history. In addition, the person signing the consent form will receive a copy of the consent form. The study staff will sign the consent after it has been returned to the site and a copy of the signed consent by subject or legal authorized representative (LAR) and staff will be sent back to the subject or LAR via email (pdf version). Data collection will not begin until the consent has been signed by both the subject or LAR and site staff.

For the retrospective portion of the clinical study, the data will be obtained from the subject's medical records and recorded on the appropriate CRF. Data will be collected from the first patient treated (06/03/2015) to the last patient treated (09/20/2017) with the MyVaccx™ therapy. For the prospective portion of the clinical study, information will be obtained from the subjects' records as they receive standard of care according to the physician judgement for this patient population (Adenocarcinoma) and recorded on the Follow-up CRF. For the retrospective portion of the clinical study, the data will be collected from the medical records and will continue to be reviewed for the life of the subject.

RISK/SAFETY INFORMATION

There are non-physical risks associated with taking part in this study, such as the risk of accidental disclosure of your personally identifiable medical information.

MONITORING/REPORTING OF AE/SAE

The study will be monitored by Syntactx, LLC a Contract Research Organization, the following is their address and contact information.

Address:

Syntactx, LLC
4 World Trade Center
150 Greenwich Street, 44th Floor
New York, New York 10007

Contact Information:

p 212-228-9000
f 646-375-3183

STUDY OVERSIGHT

The study may be prematurely terminated by Dr. Gary Onik if the research regarding the MyVaccx™ is terminated. The study will be made available for monitoring, auditing, IRB review and regulatory inspection by providing direct access to study related source data.

DATA MANAGEMENT

The data from the approved Case Report Forms will be entered into a database (Apples Numbers) by the Clinical Research Staff. The database is password protected and has change traceability. All subjects will be given a unique identifier and all information and data concerning subjects will be considered confidential. The study results will be interpreted and summarized in a white paper by Dr. Gary Onik. All data used in the analysis and reporting of the study will be without identifiable reference to the subject.

IRB REVIEW/ETHICS/INFORMED CONSENT

The protocol, informed consent document and relevant supporting information will be submitted to the Schulman IRB for review and must be approved before the study is initiated. In addition, any subject recruitment materials will be approved by the Schulman IRB prior to being used.

This study will be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practice and applicable regulatory requirements.

The Sponsor must submit any change to the protocol to the Schulman IRB for review and approval before implementation. A protocol change intended to eliminate an apparent immediate hazard to subjects may be implemented immediately provided the Schulman IRB are notified within 10 working days.

It is the responsibility of the investigator (Dr. Gary Onik) to ensure each subject has full and adequate verbal and written information using the Schulman IRB approved informed consent document, including the objective and procedures of the study and the possible risks involved before inclusion in the study. Informed consent must be obtained prior to enrollment in the study. A copy of the signed informed consent must be given to the study subject.

Inclusion of subjects with legally authorized represntatives (LAR) who will sign the informed consent are being included to maintain data integrity to fulfill study objectives. The informed consent will not be conducted on subjects with cognitive impairment, only those subjects who are deceased will have the informed consent signed by the LAR.

CONFIDENTIALITY

Information about study subjects will be kept confidential and managed according to the requirements of the Health Insurance Portability and Accountability Act of 1996 (HIPPA). The confidentiality of the subjects will be maintained by:

1. Limiting access of study-related medical records to the monitor, auditor (if used), the Schulman IRB, and/or other regulatory authorities;
2. Maintaining confidentiality of the study-related records identifying the subject by a subject ID # on the CRF's and, to the extent permitted by applicable laws and/or regulations, will not be made publicly available;

3. Maintaining confidentiality of the subject's identity if any results of the study are published.

INTENDED USE OF THE DATA

The use of the data collected from this study will be used to write a White Paper in a standard abstract format. The White Paper will assist in writing a subsequent Prospective Study for the appropriate subjects with Adenocarcinoma.

[1] Onik GM, Bostwick DG, Miessau Esq JA, Webb Z, Friedman MB (2017) Electrical Membrane Breakdown (EMB): Preliminary Findings of a New Method of Non-thermal Tissue Ablation. J Clin Exp Pathol 7: 319. doi:10.4172/2161- 0681.1000319.