The Galvanize Therapeutics Early Stage, Non-Small Cell Lung Cancer, Treat and Resect Study

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To evaluate the safety and initial feasibility of PEF treatment of NSCLC tumors prior to surgical resection.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Respiratory and mediastinal neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON50784

Source
ToetsingOnline

Brief title
INCITE ES

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
lung cancer, Non-Small cell lung carcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Galvanize Therapeutics Inc.
Source(s) of monetary or material Support: Galvanize Therapeutics;Inc.

Intervention

Keyword: Initial feasibility, NSCLC tumor, Pulsed Electric Field (PEF) treatment, Safety

Outcome measures

Primary outcome

The primary safety analysis will be the rate of device and/or procedure related serious adverse events (SAEs) from the initial PEF treatment through surgical resection (approximately 30 days later).

Clinical Utility will be assessed through the following measures.

• Technical success defined as the frequency with which clinician can access the index tumor and deliver PEF energy

• An assessment of the treatment zone from the resected specimen

• Changes in post-treatment blood samples compared to pretreatment samples including:

o Changes in phenotypes of lymphocytes analyzed by flow cytometry (e.g. CD3+, CD4+, CD8+, etc.)

o Changes of serum levels of cytokines and mediators by ELISA assay or other method (e.g. IL-2, IL-6, IL-10, IL-12, etc.)

• Characterization of the immunologic response in post-treatment tumor tissue samples compared to pre-treatment biopsy samples including:

o Changes in histopathological assessment of immune response (PD-1/PD-L1 marker, tumor infiltrating lymphocytes, dendritic cell population, Treg

population)

o Pre and post treatment comparison of molecular NGS analysis of tumor samples

o Histologic assessment of resected lymph nodes

Secondary outcome

Safety will also be assessed through gross and histologic assessment of the resected specimen including effects upon any adjacent bronchi and vasculature and through the collection of adverse events and serious adverse events.

AEs and SAEs will be summarized using a standard medical coding dictionary (MedDRA). AEs and SAEs will be also be summarized based on Common Terminology for Adverse Events (CTCAE) version 5.0, relatedness to the device and/or procedure, and within discrete time periods in relation to the index procedure.

Further, changes to planned surgical approach as consequence of the index procedure, 30-day surgical mortality, and percentage of surgical complications due to PEF treatment will also be collected and assessed.

Additional exploratory endpoints include:

• Post-PEF change in index tumor size (measured radiographically in 3 axial planes) compared to pre-PEF treatment CT

• Pathologic response (PR) of the index tumor at surgical resection (measured as % of viable tumor remaining)

• Assessment of pre-treatment and post PEF procedure (obtained just prior to resection) changes in bronchoalveolar lavage (BAL) samples

• Outcomes as assessed through progression free survival (PFS) and overall

survival (OS) at 12-months

Study description

Background summary

Lung cancer is the most common cancer in men and the third most common cancer in women. NSCLC is the most common type of lung cancer, accounting for roughly 84% of all lung cancer diagnoses, 40% of which present at an advanced stage [Jemal 2007], including locally advanced and metastatic disease [Cancer Facts & Figures, ACS]. Early stage NSCLCs are generally not very sensitive to chemotherapy and are treated through surgical resection with curative intent when possible. Outcomes following surgical resection for small NSCLCs are good with one-year survival rates of > 90% and five-year survival generally ranging from 50-70% [van den Berg 2015]. While surgical resection results in the best long-term outcomes for early stage NSCLC (in comparison to radiation, chemotherapy, or ablation), not all patients are candidates for the procedure due to tumor location, tumor progression, comorbidities, and other reasons leaving a significant unmet need. Available treatment options for non-surgical candidates include conventional chemotherapy, radiation, and focal ablation.

Unfortunately, despite the development of additional treatments, the overall survival rate for NSCLC has only slightly improved over the last 30 years from 13% in the 1970*s to 21.7% in 2019 [American Lung Association, State of Lung Cancer 2019]. Recently, molecular targeted therapies have shown promise in improving outcomes, however, these treatments are only beneficial in subsets of tumors with the appropriate genomic alteration. Additionally, advances in immunotherapy have highlighted the potential of immune oncology-based treatments for NSCLC, however, only a small percentage of patients actually respond to treatment. Thus, there remains a significant unmet need to provide more effective therapeutic
strategies to further improve outcome in patients with NSCLC.

The delivery of pulse electric fields (PEF) represents a novel technique that is currently being researched for several clinical indications. The delivery of PEFs can induce cell death via the delivery of high frequency short duration electrical energy which disrupts the cell membrane
and the cells* ability to maintain homeostasis. One form of PEF technology known as the NanoKnife® Tissue Ablation System (AngioDynamics Inc.) is commercially available for the surgical ablation of soft tissue and is used for the treatment of various inoperable or difficultto-reach tumors. Compared to other ablative modalities used in the lung (i.e.radio-frequency, microwave,

cryotherapy), PEF ablation can induce cell death in a non-thermal manner which has several potential benefits including an improved safety profile and ability to treat lesions near critical structures due to the preservation of the surrounding architecture including vessels, lymphatics, and the extracellular matrix.

Further, cell death induced by PEF treatment may lead to enhanced efficacy through stimulation of the body*s natural immune response. As opposed to thermal ablative mechanisms, the non-thermal cell death induced by PEFs releases a greater pool of antigens from the tumor which are accessible to cells of the immune system. Additionally, limited encapsulation and scarring of the treated area allows better access to these antigens and the tumor itself for the immune cells, potentially enhancing the body*s innate and adaptive response to the tumor. A similar but modified PEF treatment to that described herein is also being studied in the lung for a chronic bronchitis indication. A recently published study reported a very good safety profile, with significant reductions in goblet cell hyperplasia and chronic bronchitis symptoms [Valipour 2020].

In this treat and resect study, PEF energy will be delivered to a solitary, operable, NSCLC lesion prior to surgical resection. The PEF treatment will be adjunctive to standard of care treatment that the patient would normally receive for their NSCLC and occur within the usual timelines approximately 30 days from diagnostic procedure to surgical resection) for these early stage NSCLC patients. This treat and resect study design allows for an evaluation of the safety, feasibility, and initial clinical utility of the approach without impacting standard of care treatment and provides a unique opportunity to resect the tissue which has received PEF treatment to determine whether this is a viable treatment option for NSCLC patients.

Study objective

To evaluate the safety and initial feasibility of PEF treatment of NSCLC tumors prior to surgical resection.

Study design

A prospective, two-arm, non-randomized, concurrently controlled, multi-center, open-label, treat and resect study

Intervention

Treatment may be delivered via either an endoluminal (bronchoscopic) or percutaneous approach at the discretion of the clinical investigator utilizing two available device configurations:
- Endoluminal: Galvanize Aliya System with commercially available TBNA Needle

(e.g., PeriView FLEX) and RF probe electrode
- Percutaneous: Galvanize Aliya System with compatible commercially available RF needle and RF probe electrode

Study burden and risks

There are potential risks and side effects associated with the Galvanize PEF procedure.

Risks potentially associated with participation in the study include the following:
Endoluminal Procedures
• Sore throat (likely occurrence)
• Coughing (likely occurrence). Coughing up small amount of phlegm (mucous) is common for 24 hours after the procedure. Coughing may continue for more than 24 hours.
• Hemoptysis (likely occurrence)
• Infection (moderately likely occurrence) including fever, pain or soreness
• Increase respiratory symptoms (moderately likely occurrence) including shortness of breath, increased color and/or quantity of phlegm, cough, wheeze or chest tightness
• Bronchial perforation (low occurrence)
• Lung abscess (low occurrence)
• Pneumothorax (low occurrence)
• Airway stenosis, scarring or injury (low occurrence) including wheezing, hoarseness, shortness of breath and/or respiratory distress
• Significant pulmonary bleeding (low occurrence)
• Death (low occurrence)

Percutaneous Procedures
• Coughing (likely occurrence). Coughing up small amount of phlegm (mucous) is common for 24 hours after the procedure. Coughing may continue for more than 24 hours.
• Chest pain, non-cardiac (likely occurrence)
• Pneumothorax (likely occurrence),
• Air embolism (low occurrence)
• Bleeding/hemorrhage or hemothorax (low occurrence)
• Infection (moderately likely occurrence) including fever, pain or soreness
• Bronchial perforation (low occurrence)
• Lung abscess (low occurrence)
• Hemoptysis (low occurrence)
• Airway stenosis, scarring or injury (low occurrence) including wheezing, hoarseness, shortness of breath and/or respiratory distress
• Significant pulmonary bleeding (low occurrence)
• Death (low occurrence)

Other Risks

• Shortness of breath (likely occurrence)
• Gastroparesis (low occurrence)
• Abnormal cardiac rhythm function (low occurrence) including arrhythmia, atrial fibrillation, ventricular fibrillation,
• Allergic reaction (low occurrence) including abnormal breathing, difficulty swallowing, anxiety, chest pain, severe cough, lightheadedness or dizziness, sweating or fainting, swelling of the face, eyes or tongue
• Fistula (low occurrence)
• Reflex hypertension (low occurrence)
• Thrombosis (low occurrence)
• Risk of anesthesia (likely occurrence) include, nausea, vomiting, bruising at injection sites, sore throat, hoarse voice, damage to teeth, aspiration, urinary retention, myocardial infarction, respiratory failure, brain damage, and death, post bronchoscopy pain, drowsiness, slurred speech, tremor, fatigue, low blood pressure, increased carbon dioxide in your blood, slowing of the heart rate, anxiety, confusion, dizziness, shivering, bronchospasms, respiratory depression, and changes in liver or heart function.
• Death (low occurrence)

Note: *Likely occurrence* refers to risks estimated to occur in more than more than 10% of patients. Risks with *moderately likely occurrence* are estimated to occur in 1 in 100 (1%), to 1 in 10 (10%) patients. Risks with *low occurrence* are estimated to occur in less than 1 in 100 (1%) patients.

Other potential risk from study related tests and procedures include the following:
• Blood draws: Mild pain, local irritation, bleeding or bruising (a black and blue mark) at the puncture site. While rare, there is a possibility of infection or a local blood clot with any procedure in which the skin is pierced with a needle.
• CT Scan: Feeling of claustrophobia while performing the test. X-rays include some amount of radiation which may increase the risk for cancer, although unlikely.
o The effective radiation dose from one of these scans is about 4.5 mSv, which is about the same as an average person receives from background radiation in 1.2 years.
• Biopsy: Bleeding, coughing up small amounts of blood or blood-tinged sputum, pneumothorax, or scarring of the area where the biopsy was taken
• Bronchoalveolar Lavage (BAL): Risks are similar to bronchoscopy procedures including transient hypoxemia, fever, bronchospasm, and very rarely, pneumothorax

The information gained from this study could result in improved management and outcomes for NSCLC patients. No additional clinical benefit is expected beyond that which if provided through surgical resection.
While all interventional clinical studies pose some risks to study participants, the study sponsor has undertaken every effort to ensure that

risks are minimized. Based on prior literature, pre-clinical animal studies, and prior PEF clinical experience, Galvanize Therapeutics, Inc. expects the Galvanize Aliya System to be safe for the use in this clinical study.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

• Presence of solitary NSCLC nodule 8th ed. stage IA2, IA3 or IB
• Nodule measuring > 1 cm and < 4 cm diameter by CT size estimate (e.g. T1b, T1c, T2a), with a minimum 1 cm solid component
• High pre-procedure probability of malignancy as determined by the investigator
• Patient has been evaluated by a thoracic surgeon and deemed a candidate for definitive lung tissue resection

• Patient is, in the opinion of the principal investigator, able to adhere to and undergo bronchoscopy, surgical procedure and post-treatment care

Exclusion criteria

• Additional pulmonary nodules requiring intervention
• Patient is receiving concurrent cancer treatment (e.g. external beam radiation therapy, brachytherapy, chemotherapy, targeted therapy, immunotherapy, other focal therapy) or has received treatment for the index tumor in the last two years
• Patient has implanted lung devices or electronic devices
• Patient has N1 disease
• Patient is immune compromised or receiving immune modulating medication
• Recurrent NSCLC within 2 years of initial definitive treatment
• Previous checkpoint inhibitor treatment for another cancer

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	15-12-2021
Enrollment:	20
Type:	Actual

Medical products/devices used

Generic name:	Galvanize Aliya System
Registration:	No

Ethics review

Approved WMO Date:	18-05-2021
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	11-10-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
ClinicalTrials.gov	NCT04732520
CCMO	NL76406.091.21