A Clinical Evaluation of the Aliya* System in Late-Stage Cancer (INCITE LS)

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To evaluate the safety and clinical utility of PEF treatment of advanced stage or metastatic cancer following progression on immunotherapy

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

Summary

ID

NL-OMON52292

Source
ToetsingOnline

Brief title
INCITE LS

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
Advanced stage or metastatic carcinoma, cancer

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Advanced or metastatic non-small cell lung cancer, Cancer progression on checkpoint inhibitor therapy, Initial feasibility, or hepatocellular carcinoma (liver cancer), Pulsed Electric Field (PEF) treatment, renal cell carcinoma (kidney cancer), Safety

Outcome measures

Primary outcome

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

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.

The primary clinical utility endpoint will be radiological assessment of response of PEF-treated tumors and lymph nodes (e.g., change in longest diameter of tumor, change in short axis of lymph node) at 90-day follow-up.

Secondary outcome

Secondary clinical endpoints include:

• Immunologic and biomarker assessments at baseline and follow-up including:

o Changes in phenotypes of lymphocytes (e.g. CD3+, CD4+, CD8+, Treg, NK, Neutrophils MDSC, etc.) and serum levels of cytokines (e.g. IL-2, IL-6, IL-10, IL-12, IFN-*) from blood samples

Other endpoints will include:

• Procedural success of accessing tumors and delivering PEF treatment.

• Duration of checkpoint inhibitor treatment beyond PEF treatment

• Patient progression free survival (PFS) at 90 days.

o PEF-treated tumor progression, new tumor appearance after PEF treatment,

transition from indeterminate to cancer of previously existing lesion

• Patient overall survival (OS) at 12 months.

• Time to focal re-intervention of PEF-treated tumor(s)

Study description

Background summary

Cancer is a major public health problem worldwide; more than 19 million new cases of cancer were diagnosed in 2020, and nearly 10 million individuals died from cancer2. Nearly 1.8 million people died of lung cancer in 2020 globally, comprising 18% of all cancer deaths4, followed by colorectal, stomach, liver and breast cancer.

Systemic treatment options for medically inoperable patients with advanced or metastatic disease include genomic-appropriate molecularly targeted therapies, immunotherapies, and conventional cytotoxic chemotherapy, either alone or in combination. It is estimated that nearly 90% of patients with metastatic non-oncogene-addicted non small-cell lung cancer (NSCLC) receive an immunotherapy agent such as anti-PD-1/L1 axis inhibitor pembrolizumab, nivolumab, atezolizumab, avelumab, or durvalumab, or anti-CTLA-4 inhibitor ipilimumab with or without histologically-specific platinum chemotherapy or targeted agent in the treatment of their cancer7. Anti-PD-1/L1 axis immunotherapies also are approved for treatment of other late-stage solid tumor malignancies including HCC and RCC after previous systemic treatment.

Immunotherapies have demonstrated higher response rates for selected metastatic cancer patients, and survival benefits 2 to 3 times longer compared to conventional cytotoxic chemotherapy8. A smaller percentage of patients have durable responses lasting longer than 2 years, with some patients exhibiting no active disease more than 5 years after initiating anti-PD-1 axis inhibitor therapy9. Unfortunately, nearly 70% of patients on an immunotherapy regimen will develop a resistance to immunotherapy and exhibit disease progression7,10. Thus, there remains a significant unmet need to provide more

effective therapeutic strategies to further improve outcome in patients with advanced and metastatic malignancies.

The delivery of pulse electric fields (PEF) represents a novel technique that is currently being researched for several clinical indications. The delivery of PEF treatment 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 difficult-to-reach tumors. Compared to other ablative modalities used in the lung (i.e., radio frequency, microwave, cryotherapy), PEF treatment can induce cell death in a non-thermal manner which has several potential benefits including an improved safety profile and ability to treat tumors near critical structures due to the preservation of the surrounding architecture including vessels, lymphatics, and the extracellular matrix.

Further, tumor cell death induced by PEF treatment may lead to enhanced immunotherapy efficacy through stimulation of the body*s natural immune response. As opposed to thermal ablative mechanisms, the non-thermal cell death induced by PEF treatment releases a greater bolus of higher quality antigens11 from the tumor which are accessible to cells of the immune system12. Additionally, limited encapsulation and scarring of the treated area allows better access to these antigens and the remnant 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 symptoms13.

In this study, patients with advanced or metastatic NSCLC, HCC, or RCC that have demonstrated at least six months of response to immunotherapy and have radiologically documented or confirmed progressive disease consisting of up to five sites of new growth, with each site of new growth being less than or equal to 2 cm in longest diameter (lymph nodes >= 15mm shortest axis), will have PEF energy delivered to the new site(s) of growth. The PEF treatment will be adjunctive to their existing immunotherapy regimen. Patients may have had any number of previous lines of therapy including radiotherapy but their most recent therapy must include immunotherapy and it is expected that patients will remain on their immunotherapy regimen for at least three months after PEF treatment delivery, if clinically appropriate. This study design allows for an evaluation of the safety of PEF treatment in this patient population and will measure the effect of PEF treatment on local control of the treated tumor(s) to determine whether this is a viable treatment option for advanced and metastatic cancer patients.

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Study objective

To evaluate the safety and clinical utility of PEF treatment of advanced stage or metastatic cancer following progression on immunotherapy

Study design

A prospective, single-arm, non-randomized, multi-center, open-label study

Intervention

Treatment may be delivered via either an endoluminal 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)
• Needle insertion point pain (likely occurrence)
• Pneumothorax (likely occurrence),
• Air embolism (low occurrence)
• Bleeding requiring intervention (low occurrence)
• Infection (moderately likely occurrence) including fever, pain or soreness
• Bronchial perforation (low occurrence)
• Target organ abscess (low occurrence)
• Hemoptysis (moderately likely occurrence)
• Hematuria (moderately likely occurrence)
• Abdominal pain (moderately likely occurrence)
• Airway stenosis, scarring or injury (low occurrence) including wheezing, hoarseness, shortness of breath and/or respiratory distress
• Transient abnormal organ function tests (moderately likely)
• 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-procedure 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.
Fluoroscopic imaging: Fluoroscopy carries some risks, as do other X-ray procedures. The radiation dose varies depending on the individual procedure. The radiation dose is expected to be low given the length of the procedures in this study. The radiation risk is usually far less than other risks not associated with radiation, such as anesthesia or sedation
• Biopsy: Bleeding, coughing up small amounts of blood or blood-tinged sputum, pneumothorax, or scarring of the area where the biopsy was taken

The information gained from this study could result in improved development of the technology as a better treatment for advanced stage or metastatic cancer following progression on immunotherapy. It is unknown if additional clinical benefit may be experienced by patients enrolled into the study following PEF treatment.
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

Public
Galvanize Therapeutics Inc.

Industrial Road 1531
San Carlos CA 94070
US
Scientific
Galvanize Therapeutics Inc.

Industrial Road 1531
San Carlos CA 94070
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

• Patient is eligible if diagnosed and currently under physician care for one of the following advanced stage or metastatic conditions:
o Stage IV non-small cell lung cancer
o Stage IV hepatocellular carcinoma
o Stage IV renal cell carcinoma
• Patient is currently receiving PD-1/PD-L1 axis immunotherapy as their most recent line of therapy, either alone or in combination with standard of care systemic therapy for their malignancy.
• Patient has exhibited at least 6 months of response to PD-1/PD-L1 axis immunotherapy regimen (defined as complete response (CR), partial response (PR), or stable disease (SD) in their index tumors per RECIST 1.1) prior to progression.
• Patient has radiologically documented or confirmed progressive disease (per RECIST 1.1) defined as a total of <= 5 new areas of growth on existing tumors and/or new tumors.
• New tumors must be <= 2cm in longest diameter. New areas of growth on existing tumors must be <= 2cm in longest diameter. Tumors and new areas of growth must be deemed suitable by the investigator for complete treatment with PEF. Pathologic lymph nodes must be >= 15mm in short axis.
• In the judgement of the investigator, the patient is able to remain on PD-1/PD-L1 axis immunotherapy for at least 3 months after PEF treatment.
• New tumors and areas of growth on existing tumors are amenable to standard of care biopsy in order to confirm disease progression.
• Patient must be willing to undergo biopsy of at least one tumor prior to PEF treatment delivery unless there is documented histological confirmation of malignancy within 4 weeks prior to PEF treatment.
• Patient refuses surgery and/or stereotactic body radiotherapy (SBRT).
• Life expectancy >= 12 weeks.

• ECOG performance status 0-1.

Exclusion criteria

• Patient has implanted lung devices or electronic devices.
• Patient is receiving bevacizumab concurrently with their PD-1/PD-L1 axis immunotherapy.
• Patient has received any prior systemic therapy (systemic chemotherapy, immunotherapy or investigational drug) in another study within 21 days prior to study enrollment.
• Patient is scheduled to receive any concurrent chemotherapy, immunotherapy, biologic or hormonal therapy for off-label cancer treatment while on this study.
• Patient has unresolved adverse reaction to immunotherapy that requires dose modification.
• Patient has received any radiation therapy within 6 weeks prior to study enrollment.
• Patient for whom the investigator considers that the PEF treatment is not in the patient's best interest.

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	25-11-2022
Enrollment:	15
Type:	Actual

Medical products/devices used

Generic name:	Galvanize Aliya System

Registration:	No

Ethics review

Approved WMO Date:	25-05-2021
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	26-01-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	05-08-2022
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	NCT04773275
CCMO	NL77026.091.21