LUNAR-4: Pilot, Single Arm, Open-Label, Multinational Study of Tumor Treating Fields (TTFields, 150 kHz) Concomitant with Pembrolizumab for the Treatment of Metastatic Non-Small Cell Lung Cancer (NSCLC) Previously Treated with a PD-1/PD-L1 Inhibitor and Platinum-Based Chemotherapy

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To test the effectiveness and safety of TTFields, delivered using the NovoTTF-200T device, concomitant with pembrolizumab in subjects with metastatic NSCLC previously treated with a PD-1/PD-L1 inhibitor and platinum-based chemotherapy

Ethical review	Approved WMO
Status	Pending
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON57019

Source
ToetsingOnline

Brief title
LUNAR-4

Condition

- Other condition

Synonym
Lung cancer, NSCLC

Health condition

longkanker

Research involving
Human

Sponsors and support

Primary sponsor: Novocure GmbH
Source(s) of monetary or material Support: industrie

Intervention

Keyword: LUNAR-4, TTFields

Outcome measures

Primary outcome

Overall survival (OS) in subjects treated with TTFields concomitant with pembrolizumab compared to OS of subjects who were treated with docetaxel alone in the LUNAR/ EF-24 study.

Secondary outcome

• Progression-Free Survival (PFS) per Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 in subjects treated with TTFields concomitant with pembrolizumab compared to PFS of subjects who were treated with docetaxel alone in the LUNAR/ EF-24 study.

• OS in subjects treated with TTFields concomitant with pembrolizumab according to PD-L1 Tumor Proportion Score (TPS).

• PFS in subjects treated with TTFields concomitant with pembrolizumab according to PD-L1 TPS.

• OS in subjects treated with TTFields concomitant with pembrolizumab according to histology.

• PFS in subjects treated with TTFields concomitant with pembrolizumab according to histology.

• Relationship between OS and PFS, and NovoTTF-200T average monthly usage in subjects treated with TTFields concomitant with pembrolizumab

• Safety profile of TTFields concomitant with pembrolizumab

Study description

Background summary

Worldwide, lung cancer is the leading cause of cancer death with an estimated 1.8 million deaths in 20201. Approximately 84% of patients with lung cancer have NSCLC and about 60% of them have distant metastases by the time of diagnosis (stage IV).
Substantial improvements in general understanding of disease biology, application of biomarkers, and refinements in treatment have led to remarkable progress and transformed outcomes for many patients. Yet, as the majority of patients unfortunately are metastatic upon diagnosis, the cure rates are low and all stages are at a high risk of relapse and progression despite modern therapy.

TTFields are a non-invasive treatment for solid tumors that is well tolerated and has been approved for the treatment of recurrent and newly diagnosed glioblastoma (GBM) and for unresectable malignant pleural mesothelioma by the Food and Drug Administration (FDA) and has obtained a CE mark in Europe for the same indication.
TTFields are delivered to the tumor site via a portable medical device that consists of a field generator and arrays that are placed on the patient*s skin. TTFields target cancer cells via multiple mechanisms, disrupting processes important for cancer cells (e.g. division and movement), which can ultimately lead to cell death over time. Additionally, TTFields have been shown to enhance antitumor immune responses.

The ability of TTFields to disrupt multiple processes in cancer cells highlights the potential of TTFields to be used with existing cancer therapies. The magnitude of the anticancer effects of TTFields is dependent on the

frequency, intensity, time, and direction of TTFields delivery, and can be modified to target a diverse range of solid tumors.

Study objective

To test the effectiveness and safety of TTFields, delivered using the NovoTTF-200T device, concomitant with pembrolizumab in subjects with metastatic NSCLC previously treated with a PD-1/PD-L1 inhibitor and platinum-based chemotherapy

Study design

Pilot, single-arm, open-label, multi-center study evaluating TTFields therapy concomitant with pembrolizumab in subjects with metastatic NSCLC whose tumors express PD-L1 (TPS >=1%), who received prior PD-1/PD-L1 inhibitor and platinum-based chemotherapy.
The number of subjects with squamous histology will be capped to a maximum of 25 (36%) subjects

Intervention

Mild to moderate dermatitis is the most common adverse event seen in subjects treated with the NovoTTF-200T Treatment Kit. In order
to prevent and treat this condition, prophylaxis and intervention recommendations are described in appendix 2 of the study protocol.

Study burden and risks

- The study takes a total of approximately 2 years for patients.
- Additional hospital visits, additional physical tests, including a pregnancy test.
-Possible inconveniences and risks associated with the research procedures:
• Blood samples: Taking blood may cause faintness and/or swelling, pain, redness, bruising, bleeding or infection (infection occurs
rare) at the site where the needle is inserted.
• Scans: Skin irritation is very rare, but can occur due to the gel used.

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

Individuals must meet all of the following inclusion criteria in order to be eligible to be enrolled and participate in the study:
1. Signed informed consent form.
a. Be >=22 years of age on the day of providing informed consent in the USA.
b. Be >=18 years of age on the day of providing informed consent outside of the USA.
2. Life expectancy of > 3 months.
3. Histologically or cytologically confirmed diagnosis of NSCLC.
4. Documented positive tumor PD-L1 expression (TPS>=1%).
5. ECOG Score of 0-1.
6. Diagnosis of radiological progression while on or after first platinum-based systemic therapy administered for advanced or metastatic disease.
Subjects should not receive any systemic therapy after PD-1/PD-L1 Inhibitor + platinum failure before enrollment into the study. Maintenance therapy after platinum-based therapy and prior to progression is allowed. Sequence or combination of PD-1/PD-L1 inhibitor and platinum-based therapy is acceptable.
7. Subjects must have received one line of PD-1/PD-L1 inhibitor therapy for advanced or metastatic NSCLC. PD-1/PD-L1 inhibitor may have been given alone or in combination with other therapy.
8. Subjects who received PD-1/PD-L1 inhibitor for advanced disease, must have

had a best response on PD-1/PD-L1 inhibitor of stable disease, partial response or complete response (in the opinion of the treating physician).
9. Subjects must have experienced disease progression (in the opinion of the treating physician) more than (>) 84 days following cycle 1 day 1 of their most recent PD-1/PD-L1 inhibitor therapy. Patients whose most recent line of therapy was PD-1/PD-L1 inhibitor monotherapy must have also experienced disease progression during or after prior platinum-based therapy.
10. Subject must have a CT with IV contrast or MRI with IV gadolinium scan of the brain to evaluate for central nervous system (CNS) disease within 28 days prior to study enrollment.
11. Adequate hematologic and end-organ function, defined by the following laboratory test results, obtained within 14 days prior to study enrollment:
I. ANC >= 1.5 x 109/L (1,500/µL) without granulocyte colony-stimulating factor support
II. Platelet count >= 100 x 109/L (100,000/µL) without transfusion
III. Hemoglobin >= 90 g/L (9 g/dL)
Subjects may be transfused to meet this criterion.
IV. AST, ALT <=2.5 × ULN (<=5 × ULN for subjects with liver metastases)
V. Bilirubin <= 1.5x ULN
VI. Calculated creatinine clearance* (CrCl) >= 15 mL/min
For subjects not receiving therapeutic anticoagulation: INR or aPTT <= 1.5 x ULN (unless subject is receiving anticoagulant therapy as long as INR or aPTT is within therapeutic range of intended use of anticoagulants).
12. A female subject is eligible to participate if she is not pregnant, not breastfeeding, and at least one of the following conditions applies:
a. Not a woman of childbearing potential (WOCBP)
b. A WOCBP who agrees to use two adequate barrier methods or a barrier method plus a hormonal method during the treatment period and for at least 120 days after the last dose of study therapy. Such methods of contraception, or true abstinence from heterosexual activity, when this is in line with the preferred and usual lifestyle of the subject, are required (periodic abstinence, e.g., calendar, ovulation, symptothermal, post-ovulation methods and withdrawal are not acceptable methods of contraception).
13. If male subject with a female partner(s) of child-bearing potential, must agree to use an effective contraception method based on the recommendation of the investigator or a gynecologist, starting with the first dose of study therapy through 120 days after the last dose of study therapy. Males with pregnant partners must agree to use a condom; no additional method of contraception is required for the pregnant partner.
Note: Abstinence is acceptable if this is the usual lifestyle and preferred contraception for the subject.
14. Able to operate the NovoTTF-200T device independently or with the help of a caregiver.
*Creatinine Clearance should be calculated using the Cockcroft-Gault Method

Exclusion criteria

All individuals meeting any of the following exclusion criteria will be excluded from study enrollment and participation:
1. Mixed small cell and NSCLC histology.
2. Subject must not have leptomeningeal disease or spinal cord compression.
3. Subject must not have brain metastases unless: (1) metastases have been locally treated and have remained clinically controlled and asymptomatic for at least 14 days following treatment, and prior to study enrollment, AND (2) subject has no residual neurological dysfunction and has been off corticosteroids for at least seven days prior to study enrollment.
4. Contra-indication for PD-1/PD-L1 inhibitor therapy.
5. Subjects must not have received more than one line of PD-1/PD-L1 inhibitor for advanced disease.
6. Subjects with a known sensitizing mutation for which an Food and Drug Administration (FDA)-approved targeted therapy for NSCLC exists (e.g., EGFR, ALK, ROS1, BRAF, RET, NTRK, KRAS, HER2 and MET sensitizing mutations), are excluded unless previously received at least one of the approved therapy(ies). Prior targeted therapy for subjects with targetable alterations is allowed if all other eligibility criteria are also met.
7. Subjects with more than (>) 2 lines of therapy in the advanced setting.
8. Had major surgery <3 weeks prior to Study enrollment.
9. Subject received lung radiation therapy of > 30 Gy within 6 months before the first dose of study treatment.
10. Has a known additional malignancy that is progressing or has required active treatment within the past 3 years.
For example: Subjects with basal cell carcinoma of the skin, squamous cell carcinoma of the skin, carcinoma in situ (e.g., breast carcinoma, cervical cancer in situ), or similar cancers that have undergone potentially curative therapy are not excluded.
11. Has active autoimmune disease that has required systemic treatment in past 2 years (i.e. with use of disease modifying agents, corticosteroids or immunosuppressive drugs). Replacement therapy (e.g., thyroxine, insulin, or physiologic corticosteroid replacement therapy for adrenal or pituitary insufficiency, etc.) is not considered a form of systemic treatment.
12. Has a diagnosis of immunodeficiency or is receiving chronic systemic steroid therapy (in dosing exceeding 10 mg daily of prednisone equivalent) or any other form of immunosuppressive therapy within 7 days prior study enrollment. Subjects with asthma that require intermittent use of bronchodilators, inhaled steroids, or local steroid injections would not be excluded from the study.
13. Significant comorbidity which is expected to affect the subject*s prognosis or ability to receive the study therapy:
a. History of significant cardiovascular disease unless the disease is well controlled.
Significant cardiac disease includes second/third-degree heart block;

significant ischemic heart disease; poorly controlled hypertension; congestive heart failure of the New York Heart Association (NYHA) Class II or worse (slight limitation of physical activity; comfortable at rest, but ordinary activity results in fatigue, palpitation or dyspnea).
b. History of arrhythmia that is symptomatic or requires treatment. Subjects with atrial fibrillation or flutter controlled by medication are not excluded from participation in the study.
c. Any serious underlying medical condition (including active infection) that would impair the ability of the subject to receive protocol therapy.
d. History of any psychiatric condition that might impair the subject*s ability to understand or comply with the requirements of the study or to provide consent.
e. Known medical condition that, in the investigator*s opinion, would increase the risk associated with study participation or study drug administration or interfere with the interpretation of safety results.
14. Subject must not be receiving or planning to receive another investigational therapy during study participation.
15. Implantable electronic medical devices (e.g. pacemaker, defibrillator) in the upper torso.
16. Known allergies to medical adhesives or hydrogel.
17. Admitted to an institution by administrative or court order.

Study design

Design

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	10-09-2024
Enrollment:	2
Type:	Anticipated

Medical products/devices used

Generic name:	NovoTTF-200T
Registration:	No

Ethics review

Approved WMO Date:	18-09-2024
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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
CCMO	NL86731.000.24