LUNAR: pivotal, randomized, open-label study of Tumor Treating Fields (TTFields) concurrent with standard of care therapies for treatment of stage 4 non-small cell lung cancer (NSCLC) following platinum failure

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To test the efficacy and safety of TTFields, using the NovoTTF-200T System, concurrent with standard therapies for stage 4 NSCLC patients, followingprogression while on or after platinum based treatment

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

Summary

ID

NL-OMON53129

Source
ToetsingOnline

Brief title
LUNAR EF-24

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
lung cancer, non-small cell lung cancer (NSCLC)

Research involving

Human

Sponsors and support

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

Intervention

Keyword: Lung cancer, NSCLC, Tumor Treating Fields

Outcome measures

Primary outcome

Overall Survival (OS) of patients treated with TTFields + docetaxel or immune checkpoint inhibitors Vs. docetaxel or immune checkpoint inhibitors alone (Superiority analysis)

Secondary outcome

Key secondary endpoints:

- Overall Survival of patients treated with TTFields + Docetaxel Vs. Docetaxel alone (Superiority analysis)

- Overall Survival of patients treated with TTFields + Immune checkpoint inhibitors Vs. immune checkpoint inhibitors alone (Superiority analysis)

Additional secondary endpoints:

- Overall Survival of patients treated with TTFields + Docetaxel Vs. immune checkpoint inhibitors alone (non-inferiority analysis)

- Progression-free survival of patients treated with Docetaxel or Immune

checkpoint inhibitors + TTFields vs. Docetaxel or Immune checkpoint inhibitors alone, based on RECIST criteria

- Overall radiological response rate (based on RECIST criteria) of patients treated with Docetaxel or Immune checkpoint inhibitors + TTFields vs. Docetaxel or Immune checkpoint inhibitors alone.

- Quality of life of patients treated with docetaxel or Immune checkpoint inhibitors concomitant with TTFields compared to that of patients who are treated with docetaxel or Immune checkpoint inhibitors without TTFields, using the EORTC QLQ C30 questionnaire with LC13 addendum.

- Analyses of the effects of NovoTTF-200T with each type of immune checkpoint inhibitor on OS and PFS

- Analysis of the effects of NovoTTF-200T on OS and PFS within each histological subgroup (squamous and non-squamous)

- The effect of treatment usage time with NovoTTF-200T (as calculated from the device log file) to check whether average monthly usage time of over 75% of the time leads to better OS and PFS outcomes, as seen in glioblastoma patients treated with TTFields

- Adverse events, severity and frequency, in patients treated with docetaxel or

Immune checkpoint inhibitors concomitant with TTFields using the NovoTTF-200T

System compared to patients treated with docetaxel or Immune checkpoint

inhibitors alone

Study description

Background summary

In a single arm pilot study (phase I/II), 42 inoperable stage IIIB (with pleural effusion) and IV NSCLC patients who had had tumor progression after at least one line of prior chemotherapy received pemetrexed 500mg/m2 intravenously every 3 weeks together with continuous daily 150 kHz TTFields (for 12 hours per day) applied to the chest and upper abdomen until disease progression. The primary endpoint was time to "in-field" progression. Median age was 63 years, 76 % had stage IV disease, 78% had adenocarcinoma and 17% had an Eastern Cooperative Oncology Group (ECOG) performance status of 2.

The median time to in-field progression was 28 weeks and the median time to progression was 22 weeks. Six patients (14.6 %) had a partial response (PR) and 20 (48.8%) had stable disease (SD). The median overall survival was 13.8 months (compared to the historical control of 8.3 months reported in the phase III trial of pemetrexed alone compared to docetaxel) and the 1 year survival rate was 57% (compared to the historical control of 30% reported for pemetrexed alone). Given that it is now known that pemetrexed has no benefit for squamous histology, it is interesting to note that in an exploratory analysis of histology subsets, patients with tumors of adenocarcinoma histology had an overall survival of 12.8 months (n=35) and patients with tumors of squamous cell histology had an overall survival of 13.8 months (n=7). The combination was well tolerated and, compared to a pemetrexed historical control, there was no increase in the adverse event rate, GI toxicity or hepatic toxicity and no device related cardiac arrhythmias were reported. There were also no TTFields-related serious adverse events. The only device-related adverse event was mild to moderate contact dermatitis in 14 patients, which was expected with use of the transducer arrays. Therapy usage time was very good with 85% of patients adhering to the recommended TTFields schedule.

The hypothesis of this study is that the use of TTFields concurrent to standard of care therapies in stage 4 NSCLC after platinum failure will increase overall survival compared to patients receiving standard therapies alone.

Study objective

To test the efficacy and safety of TTFields, using the NovoTTF-200T System, concurrent with standard therapies for stage 4 NSCLC patients, following progression while on or after platinum based treatment

Study design

Pivotal, randomized, open-label study of Tumor Treating Fields (TTFields) concurrent with standard of care therapies for treatment of stage 4 non-small cell lung cancer (NSCLC) following platinum failure

Intervention

Each patient has 50% chance of being enrolled into one of the following two groups:

• The TTFields group: Patients receive chemotherapy or immunotherapy with TTFields

-OR-

• The control group: Patients only receive chemotherapy or immunotherapy

Your study doctor will choose between the standard care consisting of docetaxel chemotherapy or immunotherapy with a PD- L1/PD-1 inhibitor (Atezolizumab, Nivolumab of Pembrolizumab) according to the best practices of the institution with appropriate premedication. These medicines are approved for the treatment of your disease and are administered at their standard dose at standard frequency.

Chemotherapy or immunotherapy is administered intravenously (injection in the vein) at the hospital or the clinic. Your doctor may prescribe other medications for or after your chemotherapy to prevent side effects. Your doctor will decide how long you will be treated with chemotherapy or immunotherapy.

Study burden and risks

TTFields:
The treatment with the NovoTTF-200T may cause localized skin irritation, skin breakdown or infection at the sites where the electrodes are in contact with skin; if this happens, the patient will be evaluated and treated by the doctor and he/she should heal completely after the treatment has been stopped. Additionally, the treatment with TTFields may not delay tumor progression or cause regression.

Other potential risks of an electric device, such as the Novo TTF-200T, are the risk of electric or mechanical faults, electric shocks and electromagnetic interference (generating electromagnetic fields that may influence other components within the device or other devices). However, Novocure has taken

appropriate precautions to limit the chance of these risks.

The device is safe and very unlikely to form a risk to others. It should not interfere with the operation of other normal electronic devices.
Other currently unknown risks and discomforts may occur. This is why it is very important that any new health problems are reported to the investigator as soon as possible.

The possible risks and discomforts of chemotherapy, immunotherapy and the assessments are available in Appendix D of the ICF.

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

1. 18 years of age and older
2. Life expectancy of >= 3 months
3. Histological or cytological diagnosis of squamous or non-squamous, inoperable, metastatic NSCLC.
4. Diagnosis of radiological progression while on or after first platinum-based systemic therapy administered for advanced or metastatic disease
a. Patients who received adjuvant or neoadjuvant platinum-based chemotherapy (after surgery and/or radiation therapy) and developed metastatic disease within 6 months of completing therapy are eligible.
b. Patients with metastatic disease more than 6 months after adjuvant or neoadjuvant platinum-based chemotherapy, who also subsequently progressed during or after a platinum- based regimen given to treat the advanced or metastatic disease, are eligible.
c. Patients should not receive any systemic therapy after platinum failure before enrollment into the study. Maintenance therapy after platinum based therapy and prior to progression is allowed.
5. ECOG Score of 0-2
6. Assigned by the physician to receive either docetaxel or immune checkpoint inhibitor per standard of care regimens
7. Able to operate the NovoTTF-200T device independently or with the help of a caregiver
8. Signed informed consent for the study protocol

Exclusion criteria

1. Metastases to central nervous system (CNS) with clinical symptoms or evidence of new metastases to CNS during screening. Patients who previously received treatments for the metastases to CNS, are stable and meet the following requirements are allowed to be enrolled:
a. The patients are neurologically returned to baseline (except for residual signs or symptoms related to CNS treatment).
b. No treatment for the metastases to CNS during the screening period (e.g. surgery, radiotherapy, corticosteroid therapy- prednisone > 10 mg/day or equivalent).
c. No progress in CNS lesions as indicated by MRI within 14 days prior to randomization.
d. No meningeal metastasis or spinal cord compression.
2. Patients planned to receive immune checkpoint inhibitor with contra-indications to receive immunotherapy
3. Patients planned to receive docetaxel with contra- indications to receive docetaxel
4. Severe comorbidities:

- a. Clinically significant (as determined by the investigator) hematological, hepatic and renal dysfunction, defined as: Neutrophil count < 1.5 x 10 9/L and platelet count < 100 x 10 9/L; bilirubin > 1.5 x ULN; AST and/or ALT > 2.5 x ULN or > 5 x ULN if patient has
documented liver metastases; and serum creatinine > 1.5 x ULN.
b. 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).
c. History of arrhythmia that is symptomatic or requires treatment. Patients with atrial fibrillation or flutter controlled by medication are not excluded from participation in the study.
d. History of pericarditis
e. History of interstitial lung disease
f. History of cerebrovascular accident (CVA) within 6 months prior to randomization or that is not stable.
g. Active infection or serious underlying medical condition that would impair the ability of the patient to receive protocol therapy.
h.History of any psychiatric condition that might impair patient's ability to understand or comply with the requirements of the study or to provide consent.
i. Any other malignancy requiring anti-tumor treatment in the past three years, excluding treated stage I prostate cancer, in situ cervical cancer, in situ breast cancer and nonmelanomatous skin cancer.
5. Concurrent treatment with other experimental treatments for NSCLC while on the study
6. Implantable electronic medical devices (e.g. pacemaker, defibrilator) in the upper torso
7. Known allergies to medical adhesives or hydrogel
8. Pregnancy or breast-feeding (patients with reproductive potential must use effective contraception methods throughout the entire study period, as determined by their investigator/gynecologist)
9. Admitted to an institution by administrative or court order

Study design

Design

Study phase:	3
Study type:	Interventional

Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	05-10-2018
Enrollment:	10
Type:	Actual

Medical products/devices used

Generic name:	NovoTTF-200T System
Registration:	No

Ethics review

Approved WMO Date:	23-01-2018
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	09-03-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	14-10-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	07-12-2020

Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-02-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	26-07-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	31-10-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NCT02973789
CCMO	NL61747.078.17