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Radiation treatment followed by benmelstobart injection plus anlotinib before surgery for people with stage two to stage three epidermal growth factor receptor–positive non–small cell lung cancer

Submission date
28/01/2026

Recruitment status
Recruiting

Registration date
02/02/2026

Overall study status
Ongoing

Last Edited
02/02/2026

Condition category
Cancer

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims

Non–small cell lung cancer is the most common type of lung cancer. For patients with stage II to stage III driver gene–negative non–small cell lung cancer, the current standard treatment is chemotherapy combined with immunotherapy followed by curative-intent surgery. However, for patients with epidermal growth factor receptor mutations, there is no established standard neoadjuvant treatment regimen. This study aims to explore the efficacy and safety of stereotactic body radiation therapy followed sequentially by Benmelstobart Injection combined with anlotinib as neoadjuvant treatment for stage II to stage III epidermal growth factor receptor–positive non–small cell lung cancer.

Who can participate?

Adults (men or women) aged 18 years or older may be able to take part if they:

1. Have previously untreated stage two to stage three non–small cell lung cancer confirmed by a tissue or cell sample.
2. Have a confirmed epidermal growth factor receptor mutation.
3. Have lung disease that a multidisciplinary team (including thoracic surgeons) considers resectable or potentially resectable.
4. Are generally fit and active, with an Eastern Cooperative Oncology Group performance status of 0 to 1.

What does the study involve?

This is a single-group (single-arm), phase two, multicenter clinical study, meaning all participants receive the same study treatment and there is no comparison group. The planned total number of participants is 49, across multiple hospitals.

After signing the informed consent form and being confirmed as eligible according to the inclusion and exclusion criteria, participants will receive a 3-day course of stereotactic body

radiation therapy (8 Gy per day). Within 7 days after completing stereotactic body radiation therapy, participants will receive 2 to 3 cycles of Benmelstobart Injection combined with anlotinib, and curative-intent surgery will be performed 4 to 6 weeks after the final dose of Benmelstobart Injection. After surgery, follow-up will be conducted in accordance with recommendations from international guidelines.

What are the possible benefits and risks of participating?
Possible benefits:
1. The pre-surgery treatment may shrink the tumor and lymph node disease, potentially making surgery easier or more effective.
2. Participants will receive close monitoring by a specialist research and clinical team.
3. Information from this study may help improve future treatment for people with this type of lung cancer.
Possible risks:
1. Radiotherapy-related side effects, which can include tiredness, skin irritation, inflammation of the lung (which may cause cough, fever, or shortness of breath), chest discomfort, and rarely more serious lung injury.
2. Benmelstobart Injection (immunotherapy) side effects: immunotherapy can sometimes cause the immune system to attack normal organs. This may lead to inflammation in organs such as the lungs, liver, bowel, thyroid and other hormone glands, skin, or kidneys.
3. Anlotinib side effects: this type of medicine can raise blood pressure and may increase the risk of bleeding or blood clots in some people.
The study team will monitor participants closely, manage side effects promptly, and may pause or stop treatment if needed for safety.

Where is the study run from?
The study is led and coordinated by Sun Yat-sen University Cancer Center and is run across multiple hospitals in China, including: Sun Yat-sen University Cancer Center, Peking University Cancer Hospital, Cancer Hospital Shenzhen Hospital (Chinese Academy of Medical Sciences), Tangdu Hospital, Shanghai Chest Hospital, Yunnan Cancer Hospital, etc.

When is the study starting and how long is it expected to run for?
Expected study start: February 2026
Expected last participant enrolled: February 2028
Expected study end: February 2030

Who is funding the study?
Chia Tai Tianqing Pharmaceutical group Company Limited will provide the study drugs required for the research and insurance coverage for participants.

Who is the main contact?
Principal Investigator: Professor Lanjun Zhang (Sun Yat-sen University Cancer Center, e-mail address: Zhanglj@sysucc.org.cn).

Contact information

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Study information

Scientific Title
Stereotactic body radiation therapy followed sequentially by benmelstobart injection combined with anlotinib as neoadjuvant treatment for stage II to stage III epidermal growth factor receptor–positive non–small cell lung cancer: a single-arm, multicenter, phase two clinical study

Study objectives

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 27/10/2025, Ethics Committee of Sun Yat-sen University Cancer Center (NO.651, Dongfeng Road East, Guangzhou, 510060, China; +86 202-87343009; llwyh@sysucc.org.cn), ref: B2025-629-01

Primary study design
Interventional

Allocation

N/A: single arm study

Masking
Open (masking not used)

Control
Uncontrolled

Assignment
Single

Purpose
Treatment

Study type(s)

Health condition(s) or problem(s) studied
Neoadjuvant treatment for stage II-III epidermal growth factor receptor–positive non–small cell lung cancer

Interventions
After signing the informed consent form and being confirmed as eligible according to the inclusion and exclusion criteria, participants will receive a 3-day course of stereotactic body radiation therapy (8 Gy per day). Within 7 days after completing stereotactic body radiation therapy, participants will receive 2 to 3 cycles of Benmelstobart Injection combined with anlotinib, and curative-intent surgery will be performed 4 to 6 weeks after the final dose of Benmelstobart Injection. After surgery, follow-up will be conducted in accordance with recommendations from international guidelines.

Intervention Type
Mixed

Primary outcome(s)
1. pCR rate measured using pathologically assessed proportion of viable tumor cells at 1 week after surgery

Key secondary outcome(s))

Completion date
01/02/2030

Eligibility

Key inclusion criteria
1. Patients with previously untreated stage II to stage III non–small cell lung cancer confirmed by cytology and/or histology.
2. Positive for an epidermal growth factor receptor mutation.
3. Pulmonary lesions considered resectable or potentially resectable after discussion by a multidisciplinary team with thoracic surgery involvement.
4. Eastern Cooperative Oncology Group performance status score of 0 to 1.

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 years

Upper age limit
75 years

Sex
All

Total final enrolment
0

Key exclusion criteria
1.The patient has, or is suspected of having, an autoimmune disease.
2.The patient is expected to require systemic corticosteroid therapy within 14 days after enrollment.
3.Patients with grade 3 to 4 interstitial lung disease.
4.Concurrent other malignancy requiring antitumor treatment.
5.Imaging (computed tomography or magnetic resonance imaging) shows that the tumor lesion is within 5 millimeters of a major blood vessel, invades local major blood vessels, or is a central tumor located within 2 centimeters of the bronchus; or there is an obvious cavitary or necrotic lung tumor.
6.Clinically significant hemoptysis within 2 weeks prior to enrollment (more than 50 milliliters per day) or other clinically significant bleeding symptoms, or a definite bleeding tendency.
7.Imaging shows tumor involvement around critical vessels, or in the investigator’s judgment the tumor is highly likely to invade critical vessels during the study, posing a risk of fatal massive hemorrhage.
8.Arterial or venous thrombotic events within the past 6 months, such as cerebrovascular accident (including transient ischemic attack), deep vein thrombosis, or pulmonary embolism.

Date of first enrolment
01/02/2026

Date of final enrolment
01/02/2028

Locations

Countries of recruitment
China

Sponsor information

Organisation
Sun Yat-sen University Cancer Center

ROR
https://ror.org/0400g8r85

Funder(s)

Funder type

Funder Name
Chia Tai Tianqing Pharmaceutical group Company Limited

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available