A Phase III Randomized Trial of Adjuvant Chemotherapy With or Without Bevacizumab for Patients With Completely Resected Stage IB ($\geq$ 4 cm)–IIIA Non–Small Cell Lung Cancer (NSCLC)

Have you had or do you plan to have surgery for non–small cell lung cancer (NSCLC)?

If so, you may benefit from additional treatment.
What does it mean to be diagnosed with NSCLC?

NSCLC is a type of cancer that develops in the lung. It is a very common cause of cancer in both men and women and is the leading cause of cancer death for both.\textsuperscript{1,2} However, when NSCLC is caught early, surgery and additional treatment like chemotherapy can cure some people.

What do doctors mean when they talk about the stages of NSCLC?

Once your doctor has confirmed a diagnosis of NSCLC, the disease is “staged” using the TNM system, which evaluates whether the disease is confined to the tumor site (T), has spread to the lymph nodes (N, tissue mass that helps fight infection; located in armpit and other areas of body), or has metastasized (M, spread to another part of the body). Stage numbers (I-IV) denote the extent of disease. Staging helps identify the treatment option right for you.\textsuperscript{3}

What are my treatment options? If I’ve had surgery, isn’t that enough?

Treatment options are based on disease stage and patient characteristics (especially at more advanced stages). For patients with earlier-stage NSCLC, surgery may be enough. Research has shown that as the disease advances, more therapy beyond surgery is needed to slow or prevent the return of disease. The
standard treatment for stage IB NSCLC is surgery, but for large IB tumors *adjuvant chemotherapy* (chemotherapy given after surgery) is often considered; for stages II through IIIA, adjuvant chemotherapy is also given. 

**What is a clinical study?**

A clinical study is a way to investigate whether a new therapy is effective. Clinical studies follow tightly regulated and careful procedures to protect patients and improve the treatment of diseases. In phase III studies (like the E1505 study), patients are randomly assigned to different treatment groups to compare the treatment effects.

**What does it mean to be randomized?**

Being *randomized* means that you are assigned to a treatment group (arm) by chance. You will have an equal chance of being placed in either arm. You and your study doctor will *not* be able to choose which arm you will be in. However, you and the doctor will be able to choose your chemotherapy regimen within the arm you’re assigned to.

**Why is the E1505 study being done?**

This research is being done because even with the most aggressive after-surgery treatment with chemotherapy, the lung cancer often returns. This study will help determine if adding the drug *bevacizumab* to chemotherapy helps slow or prevent the disease from returning in patients who have had NSCLC surgery. It will compare the effects of adding bevacizumab to chemotherapy with the effects of chemotherapy alone.

This study offers 4 chemotherapy options. The standard form is cisplatin plus vinorelbine, already shown to improve the survival of patients with earlier NSCLC surgery. The 3 other treatment options (cisplatin plus either docetaxel, pemetrexed, or gemcitabine) are proven to be at *least* as active as cisplatin plus vinorelbine for metastatic lung cancer. Because they work as well as the standard option (cisplatin plus vinorelbine) for metastatic disease, most doctors believe they will work just as well as the standard option (cisplatin plus vinorelbine) for adjuvant chemotherapy too. Adjuvant chemotherapy is chemotherapy given after surgery at a time when a patient has no known disease in the body. Adjuvant chemotherapy is
given to make it less likely that a cancer will come back. This is different than chemotherapy given for metastatic disease when the cancer can be seen and the doctor can tell directly if the chemotherapy is working or not.

**How many people will take part in the E1505 study?**

About 1500 people in North America and Europe will take part in this study.

**Who can participate in the E1505 study?**

The requirements for participating are as follows:

- NSCLC completely removed by a surgeon between 42 and 84 days before being assigned to a treatment group
- No prior chemotherapy
- No hormonal cancer or radiation therapy within the past 5 years
- No history of cancer within the past 5 years
- Aged at least 18 years

*Note: A new risk of ovarian failure has been added; accrual of premenopausal women should be suspended until a revised consent adding this risk is reviewed and approved by the IRB*

Patients will be excluded from participating if they have had

- Certain types of surgery for NSCLC with partial lung removal
- Serious nonhealing wounds
- Recent major surgical procedure (less than 28 days previously) or core biopsy (less than 7 days previously)
- Uncontrolled high blood pressure (must be less than or equal to 150/90)
- Heart attack or blood clots in the arteries within the past year; any history of stroke
- Continued coughing up blood after surgery

These are the main requirements only. Your doctor will perform a more detailed review of your eligibility.
Why is bevacizumab being added to adjuvant chemotherapy in one of the treatment arms in this study?

In some patients who have surgery to remove NSCLC, the cancer later returns. In most of these patients, the tumor grows and spreads (metastasizes), which requires a steady blood supply. Bevacizumab is a drug that stops the growth of new blood vessels needed for tumor growth and spread, thus choking off the blood supply. Bevacizumab is investigational, which means it has not been approved by the FDA for use in this form of cancer. It is approved for use in advanced lung and colon cancer.\(^7,8\)

What does the study involve, in terms of procedures, time, and travel?

It is recommended that patients follow this schedule:

- **Chemotherapy**
  - Physical examination every 3 weeks during treatment
  - Posttreatment physical examinations continue every 3 months for up to 1 year

- **Chemotherapy and bevacizumab**
  - Physical examination every 3 weeks initially during combined chemotherapy and bevacizumab, then every 6 weeks while on bevacizumab alone; vital signs and an assessment of how you are feeling will be done prior to beginning each treatment; extra labs are obtained every 6 weeks while on bevacizumab alone
  - Posttreatment physical examinations continue every 3 months for up to 1 year

- **Chest x-ray** every 3 months for the first 2 years from study entry, then every 6 months during years 2-5, then annually to year 10

- **If NSCLC returns,**
  - Staging—CT scan of chest, abdomen, or pelvis; brain imaging; bone scan (or PET)
  - Biopsy is encouraged

- **Smoking survey** before treatment, then every 3 months for up to 1 year; may require a urine dipstick test (helps study effects of smoking)
• Patients in arm A (chemotherapy) will receive active treatment for about 3 months
• Patients in arm B (chemotherapy and bevacizumab) will receive active treatment for about 1 year
• Information about your health will be collected for approximately 10 years and used to determine the effectiveness and any long-term toxicity of the therapy

What can I expect to experience during the study?

Chemotherapy and bevacizumab treatments have had side effects in patients with NSCLC and other diseases.

The type of side effects depends on which of the 4 chemotherapy regimens your doctor chooses. For bevacizumab, the most commonly reported side effects include

• High blood pressure
• Abnormal levels of protein in the urine (may indicate kidney damage)
• Mild to moderate bleeding in the gastrointestinal tract (serious and life-threatening bleeding events were rare)

Your doctor will discuss potential side effects of chemotherapy and bevacizumab with you. Managing potentially severe effects is part of the plan for these treatments. In the event of severe effects, the dose may be modified.

How will I know if the treatment is helping?

The doctor visits and measurements will be an opportunity to discuss possible effects of treatment. It is important to follow your schedule so your doctor can advise you on how the treatment may be working and what is in your best interest. As with any clinical study, you are free to withdraw at any time. Open communication between you and your doctor will ensure decisions that are best for you.

If I participate, what rights do I have?

Participation in a clinical study is voluntary, and there is a process to keep you fully informed of all the facts as the study progresses. You will sign an informed consent document, which provides details about the study and what will occur.
How can I enroll?

If you would like to participate in this trial, let your doctor know. The doctor can tell you if you are eligible and supply resources for enrolling.

Who is conducting the trial?

The Eastern Cooperative Oncology Group (ECOG) is conducting this trial. ECOG is one of the largest cancer research organizations in the United States. It has a network of researchers, physicians, and health care professionals at public and private institutions across the country. ECOG conducts clinical trials in all types of adult cancers. It receives funding from the National Cancer Institute (NCI) and other sources. ECOG’s goal is to control, effectively treat, and ultimately cure cancer. ECOG provides research results to individuals and the medical community through scientific publications and professional meetings.

How can I learn more about the study?

For more information about the E1505 study, please go to the following Web sites:

- http://clinicaltrials.gov/ct/show/NCT00324805; ClinicalTrials.gov registration number: NCT00324805

For more information about ECOG, visit www.ecog.org
References


