

## **CALGB 140503:** A Randomized Phase III Trial of Lobectomy versus Sublobar Resection for Small (< 2cm) Peripheral Non-Small Cell Lung Cancer

by Nicole Fox, MD, and Thomas Bauer, MD

The surgical standard of care for early stage non-small cell lung cancer (NSCLC) is an anatomic lobectomy with mediastinal nodal staging. In 1995 the Lung Cancer Study Group (LCSG) published the results of a randomized trial in which 267 patients with peripheral T1N0 tumors were randomly assigned to lobectomy or limited resection (segmentectomy or wedge resection). The results indicated that limited pulmonary resection does not lead to improved perioperative morbidity, mortality, or late postoperative pulmonary function. There was a significantly lower rate of locoregional recurrence in the lobectomy group, although this did not translate into a statistically significant difference in overall or disease-free survival.<sup>1</sup> Based on this study, lobectomy was established as the standard of care.

Recently, however, evidence emerged that challenges the relevance of the results outlined above. Several studies suggest that survival is related to tumor size; specifically that survival is better in patients with tumors 2.0 cm or less. Port and colleagues analyzed a series of 244 patients who underwent resection for confirmed Stage 1A NSCLC.<sup>2</sup> The majority (229) of the patients underwent lobectomy. There was a statistically significant difference in survival between patients with tumors ≤ 2 cm (5 year survival of 77.2 %) as compared to patients with tumors greater than 2 cm (5 year survival of 60.3%). Another study by Gajra and colleagues also found improved survival in patients with tumors < 1.5 cm.<sup>3</sup> To date there are no prospective randomized trials; however, preliminary data from retrospective reviews support limited resection in patients with tumors 2 cm or less in size.<sup>4,5</sup> In the study conducted by Warren et al., there was no statistically significant difference in overall 5-year survival following lobectomy or segmentectomy in patients with tumors 2 cm or less.<sup>4</sup> Based on this evidence, there is clearly a need to evaluate lobectomy versus sublobar resection in this subset of tumors.

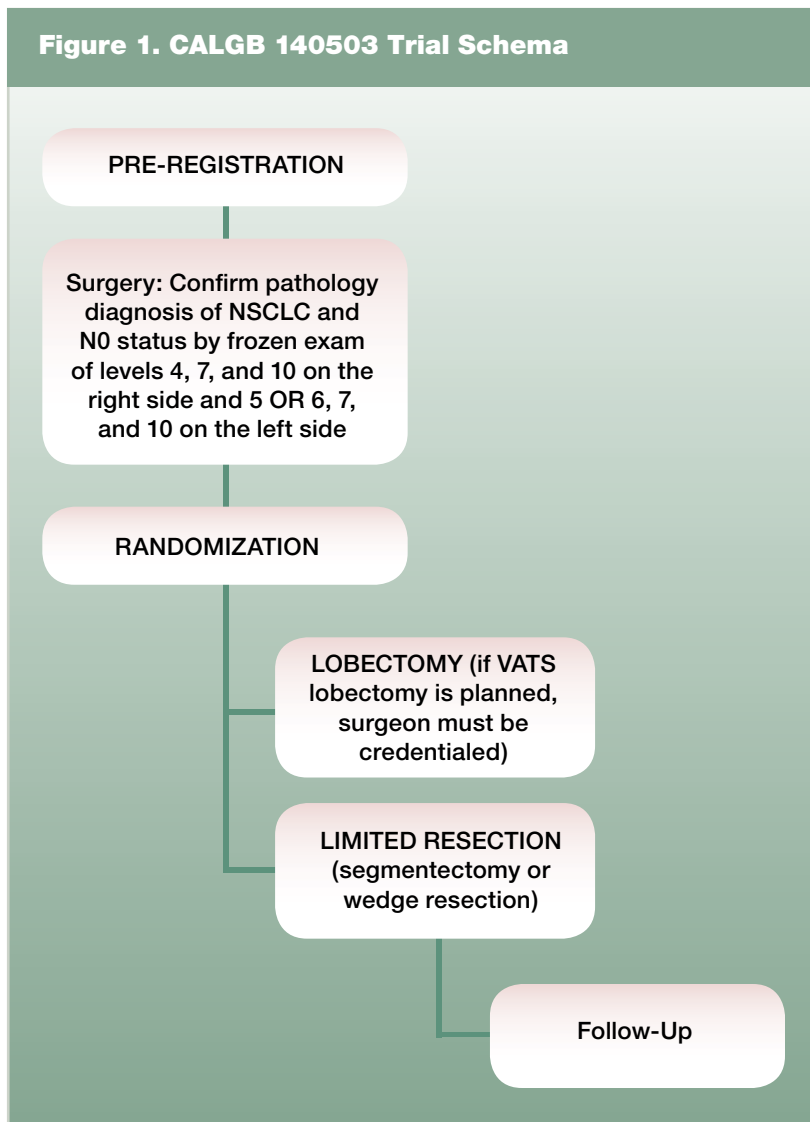
### **About CALGB 140503**

The CALGB 140503 trial is currently evaluating the potential benefit of sublobar resection for peripheral NSCLC less than or equal to 2 cm in size. The primary objective is to determine whether disease-free survival after sublobar resection (segmentectomy or wedge) is *non-inferior* to that after lobectomy in

patients with small (≤ 2cm) NSCLC. A maximum of 1,297 patients will be accrued to the study and randomized intra-operatively to either lobectomy or limited resection (see Figure 1).

**Patient Characteristics.** Prior to registration, patients must have a peripheral lung nodule measuring ≤ 2 cm on CT scan and presumed to be lung cancer. The center of the tumor as seen on CT must be located in the outer third of the lung in either the transverse, coronal or sagittal plane. Once patients meet these criteria, they will be randomized intra-operatively if there is histologic confirmation of NSCLC (if not already obtained). In addition, there must

**Figure 1. CALGB 140503 Trial Schema**



be confirmation of N0 status by frozen section examination. Nodes may be sampled at the time of operation or pre-operatively by mediastinoscopy within 6 weeks of the definitive procedure.

**Inclusion and Exclusion Criteria.** Inclusion criteria: 1) Patients with peripheral lung nodule  $\leq 2$  cm on preoperative CT scan; 2) Patients with a histologically confirmed diagnosis of NSCLC; 3) Patients with confirmed N0 status by frozen section examination; and 4) ECOG performance status of 0-2. Exclusion criteria: 1) Prior malignancy within 5 years (with the exception of non-melanoma skin cancer, superficial bladder cancer or CIS of the cervix); 2) Prior chemotherapy or radiation for this malignancy; 3) Locally advanced or metastatic disease; 4) Age  $< 18$  years.

Additional criteria are outlined in the protocol. It should be noted that the tumor location must be suitable for either lobar or sublobar resection.

**Potential Risks.** Side effects or risks associated with participation would primarily be related to the surgery. The risks of lobar or sublobar resection (as outlined in the study consent) include: air leak from operative site, cough and phlegm, pneumothorax, pneumonia, heart attack, heart failure or irregular heartbeat, infection, bleeding, poor healing, venous thromboembolism, respiratory failure requiring mechanical ventilation, leakage of fluid from the chest, injury to nerves supplying the vocal cords, stroke, and/or death.

**Planned Statistical Analysis.** Patients will be randomized equally to the two arms. A maximum of 1,297 patients will be accrued to the study with disease-free survival assessed as the primary endpoint. This gives an 80 percent

power to detect a hazard ratio of 1.3. Secondary endpoints include: overall survival, rate of locoregional and systemic recurrence, and expiratory flow rate 6 months postoperatively.

Information about the trial, contact information, and participating institutions can be found through the NCI Cancer Trials Support Unit at <http://www.ctsu.org/>.

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## References

- <sup>1</sup>Ginsberg RJ, Rubenstein LV. Randomized trial of lobectomy versus limited resection for T1N0 non-small cell lung cancer. Lung Cancer Study Group. *Ann Thorac Surg.* 1995;60(3):615-22.
- <sup>2</sup>Port JL, Kent MS, Korst RJ, et al. Tumor size predicts survival within stage IA non-small cell lung cancer. *Chest.* 2003;124(5):1828-33.
- <sup>3</sup>Gajra A, Newman N, Gamble GP, et al. Impact of tumor size on survival in stage IA non-small cell lung cancer: a case for subdividing stage IA disease. *Lung Cancer.* 2003; 42(1): 51-7.
- <sup>4</sup>Warren WH, Faber LP. Segmentectomy versus lobectomy in patients with stage I pulmonary carcinoma. Five year survival and patterns of intrathoracic recurrence. *J of Thorac Cardiovasc Surg.* 1994;107 (4): 1087-93.
- <sup>5</sup>Keenan RJ, Landreneau RJ, Maley RH, et al. Segmental resection spares pulmonary function in patients with stage 1 lung cancer. *Ann Thorac Surg.* 2004; 78(1): 228-33.

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