

# CALGB-30610

## Phase III Comparison of Thoracic Radiotherapy Regimens in Patients With Limited Small Cell Lung Cancer Also Receiving Cisplatin and Etoposide

ClinicalTrials.gov Identifier: [NCT00632853](https://clinicaltrials.gov/ct2/show/study/NCT00632853)

### Study Background

#### Trial Description

Radiation therapy uses high-energy x-rays to kill tumor cells. Drugs used in chemotherapy, such as etoposide, carboplatin and cisplatin, work in different ways to stop the growth of tumor cells, either by killing the cells or by stopping them from dividing. It is not yet known which radiation therapy regimen is more effective when given together with chemotherapy in treating patients with limited-stage small cell lung cancer. This randomized phase III trial is comparing different chest radiation therapy regimens to see how well they work in treating patients with limited-stage small cell lung cancer.

#### Arms:

Arm A - Standard Radiotherapy + Chemotherapy: (Active Comparator): Radiotherapy (every day, Monday-Friday, for a total of 3 weeks) XRT: 45 Gy BID (1.5 Gy/fx) starting on day 1 of Cycle 1 or 2, every day, for 3 weeks Chemotherapy (every 21 days for 4 cycles, for a total of 12 weeks): Cisplatin 80 mg/m<sup>2</sup> IV on day 1 OR Carboplatin AUC 5 IV day 1, every 21 days Etoposide 100 mg/m<sup>2</sup> IV Register/ on days 1, 2, and 3, every 21 days

Arm B - High Dose Radiotherapy + Chemotherapy: (Experimental): Radiotherapy (every day, Monday-Friday, for a total of 7 weeks) XRT: 70 Gy QD (2.0 Gy/fx), starting on day 1 of Cycle 1 or 2, every day, for 7 weeks Chemotherapy (every 21 days for 4 cycles, for a total of 12 weeks): Cisplatin 80 mg/m<sup>2</sup> IV on day 1 OR Carboplatin AUC 5 IV day 1, every 21 days Etoposide 100 mg/m<sup>2</sup> IV on days 1, 2, and 3, every 21 days

#### Objectives:

OUTLINE: This is a 2-part, multicenter, randomized study. Patients are stratified according to gender, weight loss 6 months prior to study entry ( $\leq 5\%$  of body weight vs  $> 5\%$  of body weight), ECOG performance status (0 vs 1 vs 2), radiotherapy technique (intensity-modulated radiotherapy vs 3-dimensional

conformal radiotherapy), radiotherapy start time (at first cycle of protocol chemotherapy, after one cycle of prior non-protocol chemotherapy vs at first cycle of protocol chemotherapy, without prior non-protocol chemotherapy vs at second cycle of protocol chemotherapy, without prior non-protocol chemotherapy) and chemotherapy backbone: carboplatin vs cisplatin.

#### OBJECTIVES:

Primary Objective: To determine whether administering high dose thoracic radiotherapy, 70 Gy (2 Gy once-daily over 7 weeks) or 61.2 Gy (1.8 Gy once-daily for 16 days followed by 1.8 Gy twice-daily for 9 days), will improve median and 2-year survival compared with 45 Gy (1.5 Gy twice-daily over 3 weeks) in patients with limited stage small cell lung cancer.

#### Secondary Objectives

1. To compare treatment related toxic effects of thoracic radiotherapy regimens in patients with limited stage small cell lung cancer
2. To compare response rates, failure-free survival and toxicity of thoracic radiotherapy regimens in patients with limited stage small cell lung cancer
3. To compare rates of local relapse, distant metastases and brain metastases with these regimens
4. To compare patients' quality of life between these treatment regimens in terms of their physical symptoms, physical functioning and psychological state
5. To describe the patterns of use of thoracic intensity modulated radiation therapy (IMRT) in patients with limited stage small cell lung cancer
6. To examine blood-based biomarkers of response and resistance to cisplatin (or carboplatin) and etoposide
7. To evaluate the correspondence between increases in plasma ProGRP concentrations and disease progression/recurrence
8. To evaluate the potential for plasma ProGRP concentrations at baseline, after each cycle of chemotherapy and at first evaluation following completion of chemotherapy to predict PFS and OS
9. To evaluate the correspondence between longitudinal decreases in plasma ProGRP concentrations and clinical response

Part 1: Patients are randomized to 1 of 3 treatment arms.

Arm I: Patients undergo standard-dose (45 Gy given in 30 treatments) thoracic radiotherapy twice daily, 5 days a week, for 3 weeks. Patients also receive cisplatin IV on day 1 or carboplatin IV and etoposide IV on days 1, 2, and 3.

Arm II: Patients undergo higher-dose (70 Gy given in 35 treatments) thoracic radiotherapy once daily, 5 days a week, for 7 weeks. Patients also receive cisplatin or carboplatin and etoposide as in arm I.

Arm III: (discontinued as of 03/10/13) Patients undergo mid-dose (61.2 Gy given in 34 treatments) thoracic radiotherapy once daily, 5 days a week, during the initial 16 days (approximately 3 weeks) of treatment and then twice daily, 5 days a week, for

the final 9 days (approximately 2 weeks) of treatment. Patients also receive cisplatin and etoposide.

In all arms, treatment with cisplatin and etoposide repeats every 21 days for 4 courses in the absence of disease progression or unacceptable toxicity.

Part 2: An interim analysis was conducted after accrual of 30 patients per arm and one experimental arm based upon a comparison of treatment-related toxicity was selected. The most toxic experimental arm was discontinued, and the trial continues comparing standard therapy (arm I) to the selected experimental regimen (arm II) as described in part 1. Please see the Arms section for more information regarding Part 2.

Prophylactic cranial irradiation (PCI): Within 3-6 weeks after completion of chemotherapy, PCI should be offered to all patients with a complete tumor response (CR) or near complete response (nCR) with only residual chest abnormalities of indeterminate nature following completion of combined modality therapy.

After completion of study treatment, patients are followed up at least every 3 months for 2 years, every 6 months for 3 years, and then annually for 5 years or until disease progression. At disease progression, patients are followed up every 6 months.

### **Study Milestones:**

Start date: March 2008

Primary Completion Date: March 2, 2022

## **Publication Information:**

Analysis Type: Primary

PubMed ID: 36623230

Citation: J Clin Oncol. 2023 May 1; 41(13): 2394-2402. Published online 2023 Jan 9.  
doi: 10.1200/JCO.22.01359

Associated Datasets: NCT00632853-D1-Dataset.csv (patients), NCT00632853-D2-Dataset.csv (ae), NCT00632853-D3-Dataset.csv (arm3)

## **Dataset Information:**

Dataset Name: NCT00632853-D1-Dataset.csv (patients)

Description: Dataset NCT00632853-D1-Dataset.csv (patients) is one of 3 datasets associated with PubMed ID 36623230. This dataset contains data presented in the publication except for most of the adverse event data.

Data can be used to approximate published study findings, but exact reproduction of previous manuscripts may not be possible in some cases (e.g., when data must be modified for de-identification purposes or have undergone further data cleaning).

Blank values indicate data not applicable or missing, except where otherwise noted.

## **NCT00632853-D1-Dataset.csv (patients) Data Dictionary:**

LABEL	NAME	ELEMENTS	COMMENTS
Patient ID	patid		
Race	race	American Indian or Alaska Native, Asian, Black or African American, More than one race, Not Reported, Unknown, White	
Ethnicity	ethnicity	Hispanic or Latino, Not Hispanic or Latino, Not Reported, Unknown	
Age (years)	age		
Number of Chemotherapy Cycles	ncycles	1, 2, 3, 4	
Treatment Arm	arm	Assigned to 45 Gy twice a day, Assigned to 70 Gy once daily	
Chemotherapy backbone	strat_chemo	Carboplatin, Cisplatin	
Radiotherapy start time	strat_cycle	At first cycle of protocol chemotherapy, without prior non-protocol chemotherapy; At first cycle of protocol chemotherapy, after one cycle of prior non-protocol	

LABEL	NAME	ELEMENTS	COMMENTS
			chemotherapy; At second cycle of protocol chemotherapy, without prior non-protocol chemotherapy
Sex	strat_sex	Female, Male	
Weight loss 6 months before study	strat_wgtloss	<=5%, >5%	
Eastern Cooperative Oncology Group performance score	strat_ps	0, 1, 2	
Radiotherapy technique	strat_rt	Intensity modulated, Three-dimensional conformal	
Received protocol therapy	rec_trt	No, Yes	
Objective response	br	Complete Response, Partial Response	
Off Treatment Reason	offreason	AEs, Alternate therapy, Completed protocol therapy, Died, Other, Patient withdrew, Physician decision, Progressive disease	
Evaluable for safety	eval_ae	No, Yes	
Radiotherapy dose	rtdose	<45 Gy, <60 Gy, =45 Gy, =70 Gy, >45 Gy, >70 Gy, 60-69 Gy	
Lost to follow-up	lostfu	No, Yes	
Withdrawn	withdrawn	No, Yes	
Overall survival status	os_stat	0=Alive, 1=Dead	

LABEL	NAME	ELEMENTS	COMMENTS
Overall survival time (months)	os_mos		This is used for "Days on study" for Table 4, however, the publication is incorrect in all but 3 patients.
Progression-free survival status	pfs_stat	0=No event, 1=Event	
Progression-free survival time (months)	pfs_mos		
Grade 5 Adverse Event	grade5ae	Adult respiratory distress syndrome, Cardiac disorder, Death NOS, Hypersensitivity, Multi-organ failure, Sepsis(gr 3/4 ANC), Sepsis(unknown ANC), Sudden death	There is one extra grade 5 adverse event reported in the data and not in the publication.
Grade 5 Adverse Event Attribution	grade5ae_att	Definite, Possible, Probable, Unlikely, Unrelated	
Completed protocol therapy (consort)	consort_comptx	0=No, 1=Yes	