



NCCTG

NORTH CENTRAL CANCER TREATMENT GROUP

Date: April 30, 2010

To: Primary Clinical Research Associates

From: Alicia Elsing
Research Protocol Specialist

Re: N0724, A Randomized Phase II Study of Oligometastatic Stage IV Non-Small Cell Lung Cancer (NSCLC) Treated with Systemic Therapy plus Either Radiotherapy to all Sites of Gross Disease or No Radiotherapy

As referenced below the following form has been updated as follows:

CRF Title	Brief Description of Edit
On-Study Form	<ul style="list-style-type: none">Added "Brain metastases" as a Descriptive Factor to page 2 of 2.

If you have any questions, please feel free to contact me at 507-538-3893 or elsing.alicia@mayo.edu.

Enclosure

North Central Cancer Treatment Group

Coordinating Group = NCCTG: N0724
SWOG: N0724

N0724: A Randomized Phase II Study of Oligometastatic Stage IV Non-Small Cell Lung Cancer (NSCLC) Treated with Systemic Therapy plus Either Radiotherapy to all Sites of Gross Residual Disease or No Radiotherapy

Addendum 3 – April 30, 2010

Summary

- In order to enhance accrual, patients being treated in any manner for brain metastases will now be eligible for this trial.
- Administrative/editorial changes.

Replacement pages are included. Please incorporate into the protocol and keep this addendum with your protocol.

Title page Updated to reflect Addendum 3 and revised NCI version date.

Protocol Resources

Page 2: **Kristine M. Hacker, R.N.** replaces ~~Dianne M. Herrera, R.N.~~ as the NCCTG Research Base Nurse.

Section 1.0 **Background**

Page 7: As a result of now allowing patients being treated for brain metastases, Section 1.19d has been revised as follows:

For patients with brain metastases as a site of oligometastatic disease, surgical resection or radiosurgery appear to prolong patient survival.^{19, 20} However, the focus of this study is to assess whether the addition of modest doses of RT to areas of gross disease will enhance the survival of patient when administered in addition to chemotherapy. Thus, patients with brain metastases will be ~~excluded~~ **included only if there were 3 lesions or fewer and they have been successfully treated without evidence of progression prior to registration on this trial.**

Section 3.0 **Patient Eligibility**

Page 8: As a result of now allowing patients being treated for brain metastases, Section 3.16 has been revised and Section 3.17 is newly added as follows:

3.16 M1 with 1-3 **non-brain** metastases but not more. Note: Patients with M1 disease that is other intrapulmonary metastases can be treated as long as the lung V20 is $\leq 40\%$.

3.17 Patients who have had up to 3 brain metastases can participate if these have been treated prior to registration and there are no signs of progression at the time of registration.

Page 9: Section 3.41 has been revised for clarification as follows:
History of **> 3** or current brain metastases **or progressive brain metastases if fewer than 3.**

Section 4.0 **Test Schedule**

Page 11: The “Arm B only:” column heading has been revised for clarification as follows:
Arm B only: **Weekly for 6 weeks** during RT

Section 5.0 **Stratification Factors**

Page 12: Section 5.4 has been revised for clarification as follows:
Histology: **Predominantly Squamous cell vs. adenocarcinoma not predominantly squamous cell NSCLC.**

Section 12.0 **Descriptive Factors**

Page 29: As a result of now allowing patients being treated for brain metastases, Section 12.4 is newly added as follows:
Brain metastases: Yes vs. no.

Section 18.0 **Records and Data Collection Procedures**

Page 38: The address for the NCCTG Operations Office has been corrected in the first sentence of Section 18.1 as follows:
...RO_FF_03_274-CC/NW Clinic...

Appendix I **Consent Form**

Page 5: The first two paragraphs under “What are the costs of taking part in this research study” section have been revised for clarification as follows:

~~You and/or your health plan will need to pay for all costs associated with this treatment. You and/or your health plan may also have to pay for other drugs or treatment that are given to help control side effects as well as the cost of tests or exams to look at possible side effects.~~

You and/or your health plan/ insurance company will need to pay for some or all of the costs of treating your cancer in this study. **You and/or your health plan may also have to pay for other drugs or treatment that are given to help control side effects as well as the cost of tests or exams to look at possible side effects.** Some health plans will not pay these costs for people taking part in studies. Check with your health plan or insurance company to find out what they will pay for. Taking part in this study may or may not cost your insurance company more than the cost of getting regular cancer treatment.

NCCTG: N0724
SWOG: N0724

North Central Cancer Treatment Group

**A Randomized Phase II Study of Oligometastatic Stage IV Non-Small Cell Lung Cancer (NSCLC)
Treated with Systemic Therapy plus Either Radiotherapy to all Sites of Gross Residual Disease or No
Radiotherapy**

*For any communications regarding this protocol,
please call the protocol resource person on the following page.*

Study Chairs: Steven E. Schild, M.D. (Research Base/Radiation Oncology)*
Mayo Clinic
13400 E Shea Blvd
Scottsdale, AZ 85259
507/538-1760
507/284-5280 (FAX)
sschild@mayo.edu

George Henning, M.D. (NCCTG/Radiation Oncology)

Study Co-chairs: Yolanda I. Garces, M.D. (Radiation Oncology)
Alex A. Adjei, M.D. (NCCTG/ Medical Oncology)
Julian R. Molina, M.D. (Research Base/Medical Oncology)
Helen J. Ross, M.D. (Research Base/Medical Oncology)
Philip J. Stella, M.D. (NCCTG/Medical Oncology)
Marie Christine Aubry, M.D. (Pathology – Mayo)
James Quesenberry, M.D. (Pathology – NCCTG)
Paul Hesketh, M.D. (SWOG/ Medical Oncology)
Laurie Gaspar, M.D. (SWOG/ Radiation Oncology)

Statistician: Nathan R. Foster, M.S. ✓
507/284-8803

***Investigator having NCI responsibility for this protocol.**

✓Study contributor(s) not responsible for patient care.

Document History	(Effective Date)
Activation	October 31, 2008
Addendum 1	May 8, 2009
Addendum 2	May 8, 2009
Addendum 3	April 30, 2010

<u>Study Participants</u>	<u>Date Activated</u>
Entire NCCTG	October 31, 2008
SWOG	Pending

NCI Version Date: April 21, 2010

Protocol Resources

	Questions:	Contact Name:
Add 1	Patient eligibility*, test schedule, treatment delays/interruptions/adjustments, dose modifications, adverse events, forms completion and submission	Rachael M. Meyers NCCTG <i>Research Base</i> Quality Assurance Specialist Phone: (507) 538-1760 Fax: (507) 284-1902 E-mail: meyers.rachael@mayo.edu
Add 3	Drug administration, infusion pumps, nursing guidelines	Kristine M. Hacker, R.N. NCCTG <i>Research Base</i> Nurse Phone: (507) 284-2459 E-mail: hacker.kristine@mayo.edu Susan Haithcox, R.N. NCCTG Member Nurse Phone: (574) 647-7977 E-mail: shaithcox@memorialsb.org
	Forms completion and submission	Christine Rogers, BS NCCTG Member Clinical Research Associate Phone: (217) 383-3394 Email: christine.rogers@carle.com
Add 1	Protocol document, consent form, regulatory issues	Alicia L. Elsing NCCTG <i>Research Base</i> Protocol Research Specialist Phone: (507) 538-3893 Fax: (507) 284-5280 E-mail: elsing.alicia@mayo.edu
	Radiation quality control	Kathryn M Scherger NCCTG <i>Research Base</i> Radiation Quality Control Coordinator Phone: (507) 266-0006 Fax: (507) 266-7240 E-mail: scherger.kathryn@mayo.edu
Add 1	Paraffin-embedded tissue pathology	Jennifer S. Mentlick NCCTG <i>Research Base</i> Pathology Coordinator Phone : (507) 293-3928 Fax : (507) 284-9628 E-mail : mentlick.jennifer@mayo.edu
	Adverse Events (AdEERS, MedWatch, Non-AER, AML/MDS)	Patricia G McNamara NCCTG <i>Research Base</i> SAE Coordinator Phone: (507) 266-3028 Fax: (507) 284-9628 E-mail: mcnamara.patricia@mayo.edu
	Technical problems with electronic form entry	Vicki Bryhn NCCTG <i>Research Base</i> Data Management Specialist Phone: (507) 266-5350 Fax: (507) 538-0906 E-mail: bryhn.vicki@mayo.edu

*No waivers of eligibility per NCI

18, 23, and 32 months from the start of their treatment.

- 1.19a In addition, Girard reported a retrospective study which included 51 patients who had resection of brain metastases.¹⁸ Chemotherapy was administered to all patients. Those having either thoracic RT or resection of the disease within the chest had a significantly longer survival compared to those only receiving chemotherapy. Prognosis mainly depended on the treatment of the lung tumor, with a marked survival advantage in the 29 patients receiving a focal treatment (thoracic surgery or radiotherapy), compared to the 22 other patients who received only chemotherapy: median, 1-year, and 2-year survival were 22.5 months, 69%, and 42%, versus 7.1 months, 33%, and 5%, respectively ($p < 0.001$).
- 1.19b This treatment strategy is a departure from the usual practice of palliative chemotherapy alone for all stage IV lung cancer patients presenting with oligometastatic disease. However, there may be a greater role for RT in select stage IV lung cancer patients. RT is currently relegated to the role of palliative therapy for symptoms in these patients. It appears that RT directed to gross disease when used with chemotherapy may extend survival compared chemotherapy alone and may render a small group of patients free of disease for an extended period of time. We propose this trial to include chemotherapy followed by RT to all sites of gross disease for patients with oligometastatic NSCLC to evaluate whether this treatment strategy will enhance the patient survival compared to historic data of patients treated with chemotherapy alone. This hypothesis is supported by 3 studies. The studies of Khan, Girard, and De Pas suggest this is true of oligometastatic advanced stage NSCLC.
- 1.19c Additionally, we would like to use PET to ensure that patients have oligometastatic disease and to aid in localization of areas of gross disease that are to be irradiated. PET data would allow us to more readily detect these sites and treat only very limited areas of the body with RT.
- 1.19d For patients with brain metastases as a site of oligometastatic disease, surgical resection or radiosurgery appear to prolong patient survival.^{19, 20} However, the focus of this study is to assess whether the addition of modest doses of RT to areas of gross disease will enhance the survival of patient when administered in addition to chemotherapy. Thus, patients with brain metastases will be included if there were 3 lesions or fewer and they have been successfully treated without evidence of progression prior to registration on this trial.
- 1.19e This study includes standard platinum based systemic chemotherapy before radiotherapy. It also allows for the use of bevacizumab during the chemotherapy (to appropriately chosen patients) and after the radiotherapy. No bevacizumab is given during radiotherapy. Sequential administration may decrease the potential for severe toxicity which can result from the use of both bevacizumab and RT. However, the literature on this issue is unclear and severe toxicity (such as hemoptysis and/or fistula formation) may occur in patients treated with bevacizumab alone or in combination with radiotherapy (either administered sequentially or concurrently).³⁵

Add 3

2.0 Goals

2.1 Primary Endpoint

- 2.11 To assess whether the addition of radiation therapy to radiographically apparent

Add 1

residual disease, after an initial course of standard chemotherapy results in an improvement in overall survival in all eligible Stage IV NSCLC patients.

2.2 Secondary Endpoint

- 2.21 To compare the following endpoints between the radiation therapy arm (Arm B) and the observation arm (Arm A) after standard chemotherapy: progression-free survival, time-to-disease progression, time-to-treatment failure, confirmed response rate, duration of response and adverse events.

3.0 Patient Eligibility

3.1 Pre-registration - Inclusion Criteria

- 3.11 ≥ 18 years of age.
- 3.12 Histologic or cytologic confirmation of Stage IV NSCLC
Note: Mixed histology allowed if all components consistent with NSCLC. In addition, patients whose tumors have squamous cell histology/feature are eligible.
- Add 1 3.13 Previously untreated disease or SD or PR ≤ 8 weeks following one previous regimen of a standard platinum-based chemotherapy given every 3-4 weeks for a total of 2-6 cycles.
- 3.14 Ability to provide informed consent.
- 3.15 Life expectancy ≥ 12 weeks.
- Add 3 3.16 M1 with 1-3 non-brain metastases but not more. Note: Patients with M1 disease that is other intrapulmonary metastases can be treated as long as the lung V20 is $\leq 40\%$.
- Add 3 3.17 Patients who have had up to 3 brain metastases can participate if these have been treated prior to registration and there are no signs of progression at the time of registration.

3.2 Pre-registration – Exclusion Criteria

- 3.21 History of or current brain metastases.
- 3.22 Second primary malignancy with the following exceptions:
 - Carcinoma in situ of the cervix.
 - Non-melanomatous skin cancer, unless that prior malignancy was diagnosed and definitively treated at least 5 years previously with no subsequent evidence of recurrence.
 - History of low-grade (Gleason score ≤ 6) localized prostate cancer even if diagnosed < 5 years prior to pre-registration.
 - Treated stage I breast cancer even if diagnosed ≤ 5 years prior to pre-registration. (The lung tumor in this case would have to be a different histology or TTF1 positive.)
- 3.23 Any prior therapies for this cancer other than 2-6 cycles of platinum-based chemotherapy. Note: bevacizumab is allowed.
- 3.24 Prior radiation therapy to the sites which need to be treated (primary lesion, clinically involved nodes, and metastatic lesions).

3.3 Randomization – Inclusion Criteria

3.31 ECOG performance status (PS) 0 or 1. (This form is now on the NCCTG website <https://ncctg.mayo.edu/ncctg/forms/NonProtocolSpecificForms/>.)

3.32 Negative pregnancy test done ≤ 7 days prior to randomization, for women of childbearing potential only.

3.33 Able to receive radiation therapy based on radiation oncology consultation.

3.34 Received at least 2-6 cycles of standard chemotherapy during or before pre-registration.

3.35 The following laboratory values obtained ≤ 21 days prior to randomization:

- PLT $\geq 100,000$ μL
- Hgb ≥ 9 g/dL
- WBC ≥ 2.0
- Creatinine ≤ 2 x UNL

Add 1

3.36 Stable Disease (SD) or Partial Response (PR).

3.4 Randomization - Exclusion Criteria

Add 3

3.41 History of > 3 or current brain metastases or progressive brain metastases if fewer than 3.

3.42 More than a minimal pleural effusion.

3.43 FEV1 < 1 Liter.

3.44 Use of supplemental oxygen on a daily basis.

3.45 Any clinically significant infection.

3.46 Unwilling to, or unable to, comply with the protocol.

Add 1

3.47 Any prior therapies for this cancer other than 2-6 cycles of platinum-based chemotherapy. Note: Prior to RT, bevacizumab is allowed until unacceptable toxicity during chemotherapy. Bevacizumab or other maintenance systemic therapy is not administered during the radiotherapy. Bevacizumab may not be administered < 4 weeks following radiotherapy (See Section 7.11). Bevacizumab or other maintenance systemic therapy may be administered again after this time until progression of disease or unacceptable toxicity.

3.48 Psychiatric illness/social situations that would limit compliance with study requirements.

3.49a Any of the following concurrent severe and/or uncontrolled medical conditions:

- Angina pectoris
- History of congestive heart failure ≤ 3 months, unless ejection fraction $> 40\%$
- Myocardial infarction ≤ 6 months prior to registration
- Cardiac arrhythmia

4.0 Test Schedule

Tests and procedures	Active Monitoring Phase			
	≤21 days prior to randomization	Arm B only: Weekly during RT	Arm A and Arm B: End of Cycle 1 ⁹	Arm A and Arm B: Observation (Every 3 months post-randomization for 1 year)
History and exam, wt, PS	X		X	X
Adverse event evaluation	X	X ⁷	X	X
Tumor assessment	X ¹			X ²
Chest CT (preferably with IV contrast) and CT at site of metastases	X ^{3,5}			X ³
Positron Emission Tomography (PET) preferably with CT	X ⁵			3 months post-randomization
MRI or CT of the head (if CT must be with contrast, contrast preferable for MRI)	X ⁵			
Hematology group WBC, Hgb, PLT	X	X	X	X
Chemistry group (creatinine, AST, ALT, total bilirubin)	X			X ⁸
Pulmonary Function Test (FEV)	X			
Pregnancy test	X ⁴			
Central Pathology Review	X ⁶			
Radiation Oncology Consult (See Section 6.65)	X			

Add 1

- Imaging studies such as chest x-ray, CT scans, PET/CT and MRIs are to be completed ≤28 days prior to randomization. Use same imaging throughout the study.
- Tumor assessment is to be completed after standard chemotherapy (i.e. prior to randomization) and during observation (every 3 months post-randomization). In addition, tumor assessments are to be completed at any time during the treatment cycle that disease progression is clinically suspected so that patient can go off treatment and receive other therapy if progression is beyond that treatable within the parameters of this trial. CT or PET/CT of body regions with known disease and radiographic studies as clinically indicated for new symptoms (headaches: MRI of brain; bone pain: MRI of bone or bone scan) at each planned follow-up until progression is determined to have occurred.
- The CT scans of the chest and mets can be eliminated if the PET is a combined PET/CT scan. CT is used for tumor measurements.
- Women of childbearing potential only. Must be done ≤7 days prior to randomization.
- Radiographic tests are to be completed ≤28 days prior to randomization.
- Diagnostic slides must be submitted ≤30 days after randomization.
- To be submitted at the end of Cycle 1 for both arms. Record worst grade for each adverse event for the entire cycle.
- Complete prior to each CT scan during observation. Creatinine must be measured prior to giving contrast for CT scan.
- For Arm A, end of Cycle 1= end of 6 weeks (42 days). For Arm B, end of Cycle 1= end of RT (21-42 days).

Add 1

Add 3

5.0 Stratification Factors *(collected at time of Randomization)*

- 5.1 Prior 1st line chemotherapy received: Bevacizumab vs. no bevacizumab.
- 5.2 Cycles of standard chemotherapy received: 2-3 vs. 4-6.
- 5.3 Linear Analogue Self Assessment value: ≤ 7 vs. > 7 .
- 5.4 Histology: Predominantly squamous cell vs. not predominantly squamous cell NSCLC.

Add 1,3

Add 1 6.0 Registration/Randomization Procedures

6.1 Pre-Registration (Step 1) – NCCTG Institutions

- 6.11 To pre-register a patient, access the NCCTG web page at <https://ncctg.mayo.edu/training> and enter the remote registration/randomization application. The remote registration/randomization application is available 24 hours a day, 7 days a week. Back up and/or system support contact information is available on the Web site. If unable to access the Web site, call the NCCTG Registration Office at (507)-284-4130 between the hours of 8 a.m. and 4:30 p.m. Central Time (Monday through Friday).

The instructions for remote registration are available on the NCCTG web page and detail the process for completing and confirming patient pre-registration. Users should refer to the section titled “Pre-Registration Components” for details on how to pre-register a patient to a study. At the time of pre-registration the patient will receive an NCCTG patient identification number. This number is to be used when submitting tissue or blood samples (See Section 17.0). **Note:** This study does not require the submission of tissue or blood at pre-registration as the pre-registration component is being used to capture patients for this study. Patient pre-registration via the remote system can be confirmed in any of the following ways:

- Contact the NCCTG Registration Office (507) 284-4130. If the patient was pre-registered, the Registration Office staff can access the information from the centralized database and confirm the pre-registration.
- Refer to “Instructions for Remote Registration” in section “Finding/Displaying Information about A Registered Subject.”

- 6.12 IRB approval(s) is required for each treating site. A signed Cancer Trials Support Unit (CTSU) IRB Certification Form is to be on file at the CTSU Regulatory Office (fax 215-569-0206). This form can be found at the following Web site: www.ctsu.org/rss2_page.asp. Guidelines can be found under Quick Fact Sheets.

In addition to submitting initial IRB approval documents, ongoing IRB approval documentation must be on file (no less than annually) at the CTSU Regulatory Office (fax 215-569-0206). If the necessary documentation is not submitted in advance of attempting patient registration, the registration will not be accepted and the patient may not be enrolled in the protocol until the situation is resolved.

When the study has been permanently closed to patient enrollment, submission of annual IRB approvals to the CTSU is no longer necessary.

- 6.13 Prior to accepting the pre-registration, the remote registration application will verify the following:
- IRB approval at the registering institution
 - Patient eligibility

- Progression (PD):

Appearance of one or more new lesions.
Unequivocal progression of existing non-target lesions.

NOTE: Although a clear progression of “non-target” lesions only is exceptional, in such circumstances, the opinion of the treating physician will prevail, and the progression status will be confirmed at a later time by the study chair or a review panel.

11.44 Overall Objective Status

The overall objective status for an evaluation is determined by combining the patient’s status on target lesions, non-target lesions, and new disease as defined in the following table.

Disease	Target Lesions	Non-Target Lesions	New Lesions	Overall Objective Status
Measurable	CR	CR	No	CR
	CR	SD	No	PR
	PR	Non-PD	No	PR
	SD	Non-PD	No	SD
	PD	Any	Yes or No	PD
	Any	PD	Yes or No	PD
	Any	Any	Yes	PD
Only Non-Measurable	---	CR	No	CR
	---	SD	No	SD
	---	Non-PD	Yes	PD
	---	PD	Yes or No	PD

11.45 Residual Disease: In some circumstances it may be difficult to distinguish residual disease from normal tissue. When the evaluation of complete response depends upon this determination, it is recommended that the residual lesion be investigated (fine needle aspirate/biopsy) before confirming the complete response status.

11.46 Symptomatic Deterioration: Patients with global deterioration of health status requiring discontinuation of treatment without objective evidence of disease progression at that time, and not either related to study treatment or other medical conditions, should be reported as PD due to “symptomatic deterioration.” Every effort should be made to document the objective progression even after discontinuation of treatment due to symptomatic deterioration:

- Weight loss >10% of body weight.
- Worsening of tumor-related symptoms.
- Decline in performance status of >1 level on ECOG scale.

11.5 Formal statistical definitions of analysis variables involving response and disease progression are contained in Section 16.0.

12.0 Descriptive Factors (collected at time of Randomization)

12.1 Number of metastatic sites at on-study: 1 vs. 2 vs. 3.

12.2 Response to initial standard chemotherapy: PR vs. SD.

12.3 Measurable disease: Yes vs. no.

12.4 Brain metastases: Yes vs. no.

Add 1

Add 1,3

18.0 Records and Data Collection Procedures

18.1 Submission Timetable

SWOG Institutions- Southwest Oncology Group members, CCOP and affiliate institutions must submit original data collection forms as listed in Section 18.0 at the required intervals directly to the NCCTG Operations Office, Attn: QAS for N0724 RO_FF_03_24-CC/NW Clinic 200 First Street Southwest, Rochester, Minnesota 55905. Please ensure that each data collection form includes a patient identification label, including the protocol number, NCCTG patient number and SWOG patient ID.

Add 1.3

Add 1

Forms	Active-Monitoring Phase (Compliance with Test Schedule)				Event-Monitoring ² (Completion of Active-Monitoring Phase)				At Each Occurrence			
	Initial Material	Pathology Review	Follow-up material		q. 3 months until PD ³	At PD ³	After PD q. 3 mos ³ until 2 years post-randomization, then q. 6 months	ADR/AER	New Primary	Grade 4 or 5 Non-AER Reportable Events/Hospitalization	Late Adverse Event	
	≤2 weeks after randomization	≤30 days after randomization	At each Evaluation (including observation)	At end of treatment								
Pre-Registration Screening Failure Form	X ⁷											
On-Study Form	X											
Baseline Adverse Events Form	X											
Path Reports	X											
Measurement Form ³	X		X ³	X ³								
Pathology Materials (See Section 17.0)		X										
RT Material ¹				X								
Event-Monitoring Form				X	X ³	X ³	X	X	X			X
Evaluation/Treatment Form			X ²	X								
Evaluation/Observation Form			X ⁴									
Nadir/Adverse Event Form			X	X								
End of Active Treatment/Cancel Notification Form	X ⁶			X								
ADR/AER (See Section 10.0)									X			
Secondary AML/MDS Report Form									X			
Notification Form										X ⁸		

Footnotes on following page.

**NCI Informed Consent Template for Cancer Treatment Trials
(English Language)**

***NOTES FOR LOCAL INVESTIGATORS: [NOTE: Retain this section and asterisk item below for NCCTG model consents]**

- The goal of the informed consent process is to provide people with sufficient information for making informed choices. The informed consent form provides a summary of the clinical study and the individual's rights as a research participant. It serves as a starting point for the necessary exchange of information between the investigator and potential research participant. This template for the informed consent form is only one part of the larger process of informed consent. For more information about informed consent, review the "Recommendations for the Development of Informed Consent Documents for Cancer Clinical Trials" prepared by the Comprehensive Working Group on Informed Consent in Cancer Clinical Trials for the National Cancer Institute. The Web site address for this document is <http://cancer.gov/clinicaltrials/understanding/simplification-of-informed-consent-docs/>
- A blank line, _____, indicates that the local investigator should provide the appropriate information before the document is reviewed with the prospective research participant.
- Suggestion for Local Investigators: An NCI pamphlet explaining clinical trials is available for your patients. The pamphlet is entitled: "If You Have Cancer...What You Should Know about Clinical Trials". This pamphlet may be ordered on the NCI Web site at <https://cissecure.nci.nih.gov/ncipubs/> or call 1-800-4-CANCER (1-800-422-6237) to request a free copy.
- Optional feature for Local Investigators: Reference and attach drug sheets, pharmaceutical information for the public, or other material on risks. Check with your local IRB regarding review of additional materials.

**These notes for {authors and} investigators are instructional and should not be included in the informed consent form given to the prospective research participant.*

Appendix I

Add 1

N0724, A Phase II Study of Oligometastatic Stage IV Non-Small Cell Lung Cancer (NSCLC) Treated with Systemic Therapy plus Either Radiotherapy to all Sites of Gross Residual Disease or No Radiotherapy

This is an important form. Please read it carefully. It tells you what you need to know about this research study. If you agree to take part in this study, you need to sign this form. Your signature means that you have been told about the study and what the risks are. Your signature on this form also means that you want to take part in this study.

This is a clinical trial, a type of research study. Your study doctor will explain the clinical trial to you. Clinical trials include only people who choose to take part. Please take your time to make your decision about taking part. You may discuss your decision with your friends and family. You can also discuss it with your health care team. If you have any questions, you can ask your study doctor for more explanation.

You are being asked to take part in this research study because you have stage IV non-small cell lung cancer (NSCLC) and you have 3 or less metastases (cancer that has spread to other parts of the body) outside of your chest.

Why is this research study being done?

The purpose of this study is to:

- Find out if radiation therapy improves the survival of patients with your type of cancer, when given after chemotherapy.
- Find out what effects (good and bad) that radiation therapy after standard chemotherapy has on you and your cancer.

For this study, one half of the patients will be given radiation therapy following standard chemotherapy.

How many people will take part in the research study?

About 98 people will take part in this study.

What will happen if I take part in this research study?

If you have never been treated for your disease, you will have an X-ray or CT scan or MRI to measure your tumor and then you will be given between two and six 3-4 week cycles of a standard platinum-based chemotherapy regimen chosen by your doctor. This chemotherapy will be given outside of this study. When you are done getting your chemotherapy you will have an X-ray or CT scan or MRI to measure your tumor. If your disease has not gotten any worse or if it is only slightly worse, you will begin this study (within the first eight weeks after your chemotherapy).

If you have already completed, within the last eight weeks, a standard platinum-based chemotherapy regimen (given as two-six 3-4 week cycles), you will have an X-ray or CT scan or MRI to measure your tumor. If your disease has not gotten any worse or if it is only slightly worse, you will begin this study.

You will be "randomized" into one of the study groups described below. Randomization means that you are put into a group by chance as in the flip of a coin. Neither you nor your doctor can choose the group you will be in. You will have an equal chance of being placed in any group.

If you are in group 1, you will be randomized to receive no radiation therapy for 6 weeks.

Add 1

If you are in group 2, you will be randomized to receive radiation therapy for 3-6 weeks.

Before you begin the study ...

You will need to have the following exams, tests or procedures to find out if you can be in the study. These exams, tests or procedures are part of regular cancer care and may be done even if you do not join the study. If you have had some of them recently, they may not need to be repeated. This will be up to your study doctor.

- Physical exam and medical history (including a visit with the radiation oncologist)
- X-ray scans (CT, MRI, and/or PET) to measure your tumors
- MRI or CT of head to look and see if the cancer has spread to the brain
- Routine blood tests
- Pregnancy test

During the study

If the exams, tests and procedures show that you can be in the study, and you choose to take part, then you will need the following tests and procedures during the study. You will need these tests and procedures that are part of regular cancer care. They are being done more often because you are in this study.

- Physical exam and medical history
- X-ray scans (CT, MRI, and/or PET) to measure your tumors
- Routine blood tests
- Central review of biopsy tissue slides

After you go on the study, slides made from your biopsy tissue taken at the time of primary diagnosis will be sent to laboratories associated with the North Central Cancer Treatment Group (NCCTG) for central review to confirm the results of your local laboratory review. This review is mandatory. These slides will be kept by the North Central Cancer Treatment Group. No further testing will be done on these slides.

If you are in group 1, you will not get any radiation therapy.

Add 1

If you are in group 2, you will get radiation therapy for 3-6 weeks (Cycle 1). If you are in this group, up to 3 additional sites that your cancer has spread to could be treated at the same time as your lung cancer.

Add 1

Add 1

After 6 weeks, you will receive no further treatment as part of the study. You will then be seen every 3 months for 1 year. It is possible that you may get maintenance chemotherapy based on the recommendation of your treating physician.

If you develop questions, concerns, or problems, you may contact your physicians and arrange for additional visits in addition to the recommended visits. If your disease grows or spreads, you and your doctor can decide whether further treatment with a different treatment program would be in your best interest.

The above is summarized in the following tables:

<p>Before the study begins</p>	<ul style="list-style-type: none"> • Physical exam and medical history (including a radiation oncology exam) • X-ray scan (CT, MRI, and/or PET) to measure your tumors • MRI or CT of head • Get routine blood tests • Pregnancy test, if applicable •
<p>Group 2 only:</p>	<ul style="list-style-type: none"> • Get routine blood tests - Weekly for 6 weeks after you begin the study
<p>Group 1 and Group 2: 6 weeks after you begin the study (end of Cycle 1)</p>	<ul style="list-style-type: none"> • Physical exam • Get routine blood tests
<p>Group 1 and Group 2: 3 months after you begin the study</p>	<ul style="list-style-type: none"> • PET scan
<p>Group 1 and Group 2: Every 3 months after you begin the study for 1 year</p>	<ul style="list-style-type: none"> • Physical exam • X-ray scans (CT, MRI, and/or PET) to measure your tumors (If needed, your study doctor may want you to have these X-rays done more often.) • Get routine blood tests

Add 1

How long will I be in the research study?

You will get no radiation therapy or radiation therapy for 3-6 weeks and will then be seen every 3 months for 1 year after being entered on the study. No matter what group you are in, we would like to keep track of your medical condition for up to five years from the time you start the study. Keeping in touch with you and checking on your condition helps us look at the long-term effects of the study.

Add 1

Can I stop being in the research study?

Yes. You can decide to stop at any time. Tell the study doctor if you are thinking about stopping or decide to stop. He or she will tell you how to stop safely.

It is important to tell the study doctor if you are thinking about stopping so any risks from the radiation therapy can be evaluated by your doctor. Another reason to tell your doctor that you are thinking about stopping is to discuss what followup care and testing could be most helpful for you.

The study doctor may stop you from taking part in this study at any time if he/she believes it is in your best interest; if you do not follow the study rules; or if the study is stopped.

What side effects or risks can I expect from being in the research study?

You may have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects. However, doctors don't know all the side effects that may happen. Side effects may be mild or very serious. Your health care team may give you medicines to help lessen side effects. Many side effects go away soon after you stop taking the study medication. In some cases, side effects can be serious, long lasting, or may never go away. There also is a risk of death, but this is quite uncommon after radiotherapy.

You should talk to your study doctor about any side effects that you have while taking part in the study.

Side Effects of Chest Radiation:

More common side effects

- Tiredness
- Hard time swallowing due to injury to the esophagus (food tube). This can be severe and lead to dehydration and an inability to eat. If this happens, a feeding tube may need to be placed into your stomach.
- Damage to the skin like a bad sunburn.
- Scarring of the lung, which can make it difficult for the lungs to work effectively, which can be life threatening.
- Any organ in the chest (heart, esophagus, skin, muscle, bone, spinal cord or lung) can be injured. This can cause a variety of side effects. Your doctor will explain these side effects based on the area that is receiving the radiation.

Rare side effects

- Life-threatening injury due to severe injury to the chest organs.
- Life-threatening complications can occur in patients who receive bevacizumab (Avastin) in addition to radiotherapy such as bleeding or perforation of a hollow organ such as the trachea (windpipe) or esophagus (swallowing tube).

Radiation side effects to other sites which will be treated because they contain cancer: These depend on the site that needs treatment but can include:

Common:

- Fatigue
- Hair loss
- Skin damage like a bad sunburn
- Nausea (feeling sick to your stomach)
- Diarrhea (loose stools)
- Low blood counts with risk of infection (low white blood cell count), tiredness and shortness of breath (low hemoglobin), bleeding problems (low platelets). You may need blood transfusions if these levels drop too low.
- Bladder irritation (urgency and frequency, if the bladder is treated)

Rare:

- Severe dysfunction of the irradiated organ such as kidney or liver problems, brain injury, or bowel injury
- Fractures
- Life-threatening complications can occur in patients who receive bevacizumab (Avastin) in addition to radiotherapy such as bleeding or perforation of a hollow organ such as the digestive organs or intestines.

Reproductive risks: You should not become pregnant or father a baby while on this study because the radiation in this study can affect an unborn baby. Women should not breastfeed a baby while on this study. It is important you understand that you need to use birth control while on this study. Check with your health care provider about what kind of birth control methods to use and how long to use them. Some methods might not be approved for use in this study. The radiation used in the study may make you unable to have children in the future.

For more information about risks and side effects, ask your study doctor.

Are there benefits to taking part in the research study?

Taking part in this study may or may not make your health better. While doctors hope platinum-based chemotherapy and radiation therapy will be more useful against cancer compared to platinum-based chemotherapy alone, there is no proof of this yet. We do know that the information from this study will help doctors learn more about platinum-based chemotherapy plus radiation therapy as a treatment for lung cancer. This information could help future cancer patients.

What other choices do I have if I do not take part in this research study?

You do not have to be in this study to receive treatment for your cancer. Your other choices may include:

- Getting treatment or care for your cancer without being in a study
- Taking part in another study
- Getting no treatment
- Getting comfort care, also called palliative care. This type of care helps reduce pain, tiredness, appetite problems and other problems caused by the cancer. It does not treat the cancer directly, but instead tries to improve how you feel. Comfort care tries to keep you as active and comfortable as possible.

Talk to your doctor about your choices before you decide if you will take part in this study.

Will my medical information be kept private?

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- NCCTG researchers
- SWOG researchers
- The National Cancer Institute (NCI) and other government agencies, like the Food and Drug Administration (FDA), involved in keeping research safe for people

Add 1

[Note to Local Investigators: The NCI has recommended that HIPAA regulations be addressed by the local institution. The regulations may or may not be included in the informed consent form depending on local institutional policy.]

What are the costs of taking part in this research study?

Add 3

You and/or your health plan/ insurance company will need to pay for some or all of the costs of treating your cancer in this study. You and/or your health plan may also have to pay for other drugs or treatment that are given to help control side effects as well as the cost of tests or exams to look at possible side effects. Some health plans will not pay these costs for people taking part in studies. Check with your health plan or insurance company to find out what they will pay for. Taking part in this study may or may not cost your insurance company more than the cost of getting regular cancer treatment.

Add 3

You will not be paid for taking part in this study.

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Web site at <http://cancer.gov/clinicaltrials/understanding/insurance-coverage>. You can print a copy of the "Clinical Trials and Insurance Coverage" information from this Web site.

Another way to get the information is to call 1-800-4-CANCER (1-800-422-6237) and ask them to send you a free copy.

What happens if I am injured because I took part in this research study?

It is important that you tell your study doctor, _____ *[investigator's name(s)]*, if you feel that you have been injured because of taking part in this study. You can tell the doctor in person or call him/her at _____ *[telephone number]*.

You will get medical treatment if you are injured as a result of taking part in this study. You and/or your health plan will be charged for this treatment. The study will not pay for medical treatment.

What are my rights if I take part in this research study?

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care. You can still get your medical care from our institution.

We will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

Who can answer my questions about the research study?

You can talk to your study doctor about any questions or concerns you have about this study. Contact your study doctor _____ *[name(s)]* at _____ *[telephone number]*.

For questions about your rights while taking part in this study, call the _____ *[name of center]* Institutional Review Board (a group of people who review the research to protect your rights) at _____ *(telephone number)*. *[Note to Local Investigator: Contact information for patient representatives or other individuals in a local institution who are not on the IRB or research team but take calls regarding clinical trial questions can be listed here.]*

Where can I get more information?

You may call the National Cancer Institute's Cancer Information Service at:

1-800-4-CANCER (1-800-422-6237) or TTY: 1-800-332-8615

You may also visit the NCI Web site at <http://cancer.gov/>

- For NCI's clinical trials information, go to: <http://cancer.gov/clinicaltrials/>
- For NCI's general information about cancer, go to <http://cancer.gov/cancerinfo/>

You will get a copy of this form. If you want more information about this study, ask your study doctor.

Signature

I have been given a copy of all _____ [insert total of number of pages] pages of this form. I have read it or it has been read to me. I understand the information and have had my questions answered. I agree to take part in this study.

Printed Participant Name: _____

Participant Signature: _____

Date: _____

Printed name of person obtaining informed consent:

Signature of person obtaining informed consent:

Date _____

Local IRB changes to this document are allowed. Sections "What are the risks of the research study" or "What other choices do I have if I don't take part in this research study?" should always be used in their entirety if possible. Editorial changes to these sections may be made as long as they do not change information or intent. If the institutional IRB insists on making deletions or more substantive modifications to these sections, they may be justified in writing by the investigator and approved by the IRB. Under these circumstances, the revised language and justification must be forwarded to the North Central Cancer Treatment Group Operations Office for approval before a patient may be registered to this study.

Consent forms will have to be modified for each institution as it relates to where information may be obtained on the conduct of the study or research subject. This information should be specific for each institution.

April 30, 2010

FORMS PACKET

N0724, A Randomized Phase II Study of Oligometastatic Stage IV Non-Small Cell Lung Cancer (NSCLC) Treated with Systemic Therapy plus Either Radiotherapy to all Sites of Gross Disease or No Radiotherapy

- Contents:
- ✓ Pre-registration (Step 1) eligibility checklist (4/30/10)
 - ✓ Randomization (Step 2) eligibility checklist (4/30/10)
 - * Forms completion instructions
 - Preregistration screening failure form (10/27/08)
 - ✓ On-study form (4/13/10)
 - Baseline adverse events form (10/1/08)
 - Nadir/adverse event form (10/1/08)
 - Evaluation form (10/1/08)
 - Evaluation/observation form (3/20/09)
 - Pretreatment RECIST measurement form (10/1/08)
 - Active monitoring RECIST measurement form (10/1/08)
 - End of active treatment/cancel notification form (5/30/08)
 - Event monitoring form (1/6/09)
 - Grade 4 or 5 non-AER reportable events/hospitalization form (3/20/09)
 - Pathology submission form (3/20/09)
 - Pathology reporting form (5/30/08)
 - Radiation therapy reporting form (3/20/09)

✓ designates revised/new forms

*Generic forms completion instructions are available on the NCCTG web site under “the CRA link in the Remote Registration and Data Entry section and are titled “Remote Data Entry Screen Instructions (Forms Completion).”

The specific forms instructions take precedence over the generic forms instructions, so it is very important to review them in addition to the generic forms instructions.

**NCI COOPERATIVE GROUP
Pre-Registration Form and Eligibility Checklist**

04/302010
Page 1 of 2

Coordinating Group Protocol Number <u> N0724 </u>	Coordinating Group Code <u> NCCTG </u>
Protocol Title <u>A Randomized Phase II Study of Oligometastatic Stage IV Non-Small Cell Lung Cancer (NSCLC) Treated with Systemic Therapy plus Radiotherapy to all Sites of Gross Residual Disease or No Radiotherapy</u>	
Patient Study ID _____	Patient Medical Record Number _____
Participating Group Code (Cooperative Group where credit will be applied) (RT) _____	
Institution Name (treating location/performance site) (RT) _____	
Institution Code (CTEP assigned number) (RT) _____	
Physician of Record (RT) _____	

NCCTG Institutions only: To register a patient, access the NCCTG web page at <https://ncctg.mayo.edu/training> and enter the remote registration/randomization application.

SWOG Institutions: Pre-registration must be done through the SWOG Data Operations Center in Seattle by phoning 206/652-2267, 6:30 a.m. to 1:30 p.m. Pacific Time, Monday through Friday, excluding holidays. The SWOG Data Operations Center will then contact the NCCTG Registration Office at (507-284-4130) to pre-register the patient.

Protocol Administration

Date Informed Consent Signed: (mm/dd/yyyy) ___/___/___	Person Completing Form (Please Print)
_____	Last Name _____
Date of Pre-Registration: (mm/dd/yyyy) ___/___/___	First Name _____
_____	Phone (____) _____
	Fax (____) _____
	Email _____

Patient Demographics/Pre-Treatment Characteristics

Patient Initials (L, F, M) _____	
Patient Birth Date: (mm/dd/yyyy) ___/___/___	Patient Gender: ___ Male ___ Female
Patient Race (check all that apply) (U.S. and Canada only)	<input type="checkbox"/> White <input type="checkbox"/> Native Hawaiian or other Pacific <input type="checkbox"/> Islander <input type="checkbox"/> Asian <input type="checkbox"/> Black or African American <input type="checkbox"/> American Indian or Alaska Native <input type="checkbox"/> Unknown: Patient is unsure of race <input type="checkbox"/> Not Reported: Patient refused or data not available
Patient Ethnicity (check one)	<input type="checkbox"/> Hispanic or Latino <input type="checkbox"/> Non-hispanic <input type="checkbox"/> Unknown: Patient is unsure of ethnicity <input type="checkbox"/> Not Reported: Patient refused or data not available
Patient's ZIP Code (USA) _____ - _____	Country of Residence (if not USA) _____
Method of Payment (check one) (U.S. only)	
<input type="checkbox"/> Private Insurance (PI) <input type="checkbox"/> Medicare (MR) <input type="checkbox"/> Medicare & Private Insurance (MRP) <input type="checkbox"/> Medicaid (MD) <input type="checkbox"/> Medicaid and Medicare (MM) <input type="checkbox"/> Military or Veterans Sponsored , Not Otherwise Specified (NOS) (MVA)	<input type="checkbox"/> Military Sponsored (including CHAMPUS & TRICARE) (MS) <input type="checkbox"/> Veterans Sponsored (MV) <input type="checkbox"/> Self pay (no insurance) (SP) <input type="checkbox"/> No means of payment (no insurance) (NP) <input type="checkbox"/> Other (OTH) <input type="checkbox"/> Unknown (UNK)

NCCTG Pre-Registration (Step 1) Eligibility Checklist N0724

04/302010

Page 2 of 2

Patient study ID number _____

Pre-Registering Group: (check one) ___ NCCTG ___ SWOG

Eligibility Check - Answer questions below (yes/no). All requirements must be confirmed. All dates are to be *mm/dd/yyyy*.

Inclusion Criteria

	Yes	No	NA
≥18 years of age. Age = _____	_____	_____	_____
Histologic or cytologic confirmation of Stage IV NSCLC Note: Mixed histology allowed if all components consistent with NSCLC. In addition, patients whose tumors have squamous cell histology/feature are eligible.	_____	_____	_____
Previously untreated disease or SD or PR ≤8 weeks following one previous regimen of a standard platinum-based chemotherapy given every 3-4 weeks for a total of 2-6 cycles.	_____	_____	_____
Ability to provide informed consent.	_____	_____	_____
Life expectancy ≥12 weeks.	_____	_____	_____
M1 with 1-3 non-brain metastases but not more. Note: Patients with M1 disease that is other intrapulmonary metastases can be treated as long as the lung V20 is ≤40%.	_____	_____	_____
Patients who have had up to 3 brain metastases can participate if these have been treated prior to registration and there are no signs of progression at the time of registration.	_____	_____	_____

All responses in above section must be "Yes."

Exclusion Criteria

	Yes	No	NA
History of or current brain metastases.	_____	_____	_____
Secondary primary malignancy with the following exceptions: <ul style="list-style-type: none"> • Carcinoma in situ of the cervix. • Non-melanomatous skin cancer, unless that prior malignancy was diagnosed and definitively treated at least 5 years previously with no subsequent evidence of recurrence. • History of low-grade (Gleason score ≤6) localized prostate cancer even if diagnosed <5 years prior to pre-registration. • Treated stage I breast cancer even if diagnosed ≤5 years prior to pre-registration. (The lung tumor in this case would have to be a different histology or TTF1 positive.) 	_____	_____	_____
Any prior therapies for this cancer other than 2-6 cycles of platinum-based chemotherapy. Note: bevacizumab is allowed.	_____	_____	_____
Prior radiation therapy to the sites which need to be treated (primary lesion, clinically involved nodes, and metastatic lesions).	_____	_____	_____

All responses in above section must be "No."

Registration Check - Answer questions below (yes/no). All requirements must be confirmed. All dates are to be *mm/dd/yyyy*.

	Yes	No	NA
Consent form signed and dated.	_____	_____	_____
Authorization for use and disclosure of protected health information (<i>USA institutions only</i>) signed and dated. If not a USA institution (<i>check NA</i>); If a USA institution - Date of authorization ___ / ___ / _____	_____	_____	_____

All responses in above section must be "Yes" unless specified as "NA."

Person pre-registering Signature _____ Registration Office specialist initials _____

Physician Signature _____ Date (*mm/dd/yyyy*) ___ / ___ / _____

**NCI COOPERATIVE GROUP
Registration Form and Eligibility Checklist**

04/302010

Page 1 of 3

NCCTG Institutions only: *To register a patient, access the NCCTG web page at <https://ncctg.mayo.edu/training> and enter the remote registration/randomization application.*

SWOG Institutions: *Registration of patients must be done through the SWOG Data Operations Center in Seattle by phoning 206/652-2267, 6:30 a.m. to 1:30 p.m. Pacific Time, Monday through Friday, excluding holidays. The SWOG Data Operations Center will then contact the NCCTG Registration Office at (507-284-4130) to register and randomize the patient.*

Coordinating Group Protocol Number <u> N0724 </u>	Coordinating Group Code <u> NCCTG </u>
Protocol Title <u>A Randomized Phase II Study of Oligometastatic Stage IV Non-Small Cell Lung Cancer (NSCLC) Treated with Systemic Therapy plus Radiotherapy to all Sites of Gross Residual Disease or No Radiotherapy</u>	
Patient Study ID _____	Patient Medical Record Number _____
Participating Group Code (Cooperative Group where credit will be applied) (RT) _____	
Institution Name (treating location/performance site) (RT) _____	
Institution Code (CTEP assigned number) (RT) _____	
Physician of Record (RT) _____	

Protocol Administration

Date of Registration/Randomization: (mm/dd/yyyy) <u> / / </u>	Person Completing Form (Please Print) Last Name _____ First Name _____ Phone () _____ Fax () _____ Email _____
--	--

Patient Demographics/Pre-Treatment Characteristics

Patient Initials (L, F, M) _____	
Patient Birth Date: (mm/dd/yyyy) <u> / / </u>	Patient Gender: <u> </u> Male <u> </u> Female
Patient Race (check all that apply) (U.S. and Canada only)	<u> </u> White <u> </u> Native Hawaiian or other Pacific Islander <u> </u> Asian <u> </u> Black or African American <u> </u> American Indian or Alaska Native <u> </u> Unknown: Patient is unsure of race <u> </u> Not Reported: Patient refused or data not available
Patient Ethnicity (check one)	<u> </u> Hispanic or Latino <u> </u> Non-hispanic <u> </u> Not Reported: Patient refused or data not available <u> </u> Unknown: Patient is unsure of ethnicity
Patient's ZIP Code (USA) _____	Country of Residence (if not USA) _____
Method of Payment (check one) (U.S. only)	
<u> </u> Private Insurance (PI) <u> </u> Medicare (MR) <u> </u> Medicare & Private Insurance (MRP) <u> </u> Medicaid (MD) <u> </u> Medicaid and Medicare (MM) <u> </u> Military or Veterans Sponsored, Not Otherwise Specified (NOS) (MVA)	<u> </u> Military Sponsored (including CHAMPUS & TRICARE) (MS) <u> </u> Veterans Sponsored (MV) <u> </u> Self pay (no insurance) (SP) <u> </u> No means of payment (no insurance) (NP) <u> </u> Other (OTH) <u> </u> Unknown (UNK)

Patient study ID number _____

Randomization Group: (check one) ___ NCCTG ___ SWOG

Eligibility Check – Answer questions below (yes/no). All requirements must be confirmed. All dates are to be mm/dd/yyyy.

Inclusion Criteria

Yes No NA

ECOG performance status (PS) 0 or 1. (This form is now on the NCCTG website.) ECOG performance status = _____	____	____	____
Negative pregnancy test done ≤7 days prior to randomization, for women of childbearing potential only. If not a woman of childbearing potential or male (check NA) If a woman of childbearing potential - Negative pregnancy test date ___/___/_____	____	____	____
Able to receive radiation therapy based on radiation oncology consultation.	____	____	____
Received at least 2-6 cycles of standard chemotherapy during or before pre-registration.	____	____	____
The following laboratory values obtained ≤21 days prior to randomization. Earliest laboratory test date ___/___/_____; latest laboratory test date ___/___/_____. NOTE: These dates pertain to the following labs only.	____	____	____
• PLT ≥100,000 µL PLT (≥100000) = _____	____	____	____
• Hgb ≥9 g/dL Hgb (≥9) = _____	____	____	____
• WBC ≥2.0 WBC (≥2.0) = _____	____	____	____
• Creatinine ≤2 x UNL Creatinine (≤2 x UNL) = _____; Creatinine UNL = _____	____	____	____
Stable Disease (SD) or Partial Response (PR).	____	____	____

All responses in above section must be “Yes” unless specified as “NA.”

Exclusion Criteria

Yes No NA

History of >3 or current brain metastases or progressive brain metastases if fewer than 3.	____	____	____
More than a minimal pleural effusion.	____	____	____
FEV1 <1 Liter.	____	____	____
Use of supplemental oxygen on a daily basis.	____	____	____
Any clinically significant infection.	____	____	____
Unwilling to, or unable to, comply with the protocol.	____	____	____
Any prior therapies for this cancer other than 2-6 cycles of platinum-based chemotherapy. Note: Prior to RT, bevacizumab is allowed until unacceptable toxicity during chemotherapy. Bevacizumab or other maintenance systemic therapy is not administered during the radiotherapy. Bevacizumab may not be administered < 4 weeks following radiotherapy (See Section 7.11). Bevacizumab or other maintenance systemic therapy may be administered again after this time until progression of disease or unacceptable toxicity.	____	____	____
Psychiatric illness/social situations that would limit compliance with study requirements.	____	____	____
Any of the following concurrent severe and/or uncontrolled medical conditions: • Angina pectoris • History of congestive heart failure ≤3 months, unless ejection fraction >40% • Myocardial infarction ≤6 months prior to registration • Cardiac arrhythmia	____	____	____
Receiving any other investigational agent which would be considered as a treatment for the primary neoplasm during RT.	____	____	____
Any of the following: • Pregnant women • Nursing women • Men or women of childbearing potential who are unwilling to employ adequate contraception	____	____	____
Prior radiation therapy to the sites which need to be treated (primary lesion, clinically involved nodes, and metastatic lesions).	____	____	____

All responses in above section must be “No.”

Patient study ID number _____

Registration Check - Answer questions below (yes/no). All requirements must be confirmed. All dates are to be *mm/dd/yyyy*.

Yes No NA

Treatment on this protocol must commence at the accruing membership under the supervision of an NCCTG or SWOG member physician.	____
Treatment (protocol radiotherapy) cannot begin prior to randomization and must begin ≤14 days after randomization.	____
Pretreatment tests/procedures (see Section 4.0) must be completed ≤21 days prior to randomization. Earliest pretreatment test/procedure date ___/___/____; latest pretreatment test/procedure date ___/___/____. NOTE: The earliest pretreatment test/procedure date must be less than or equal to the earliest laboratory test date and the latest pretreatment test/procedure date must be greater than or equal to the latest laboratory test date.	____
<p><u>Exceptions to the above dates:</u></p> <ul style="list-style-type: none"> Tumor assessment: Imaging studies such as chest x-ray, CT scans, PET/CT and MRIs are to be completed ≤28 days prior to randomization (see Section 4.0). Use same imaging throughout the study. Radiographic tests [Chest CT (preferably with IV contrast) and CT at site of metastases; Positron Emission Tomography (PET) preferably with CT; MRI or CT of the head (if CT must be with contrast, contrast preferable for MRI)] are to be completed ≤28 days prior to randomization (see Section 4.0). Earliest exception (imaging studies/radiographic) test date ___/___/____; latest exception (imaging studies/radiographic) test date ___/___/____. <p>NOTE: The CT scans of the chest and mets can be eliminated if the PET is a combined PET/CT scan. CT is used for tumor measurements.</p>	
All required baseline symptoms (see Section 10.3) must be documented and graded.	____
A NCCTG or SWOG radiation oncologist has seen the patient and confirms the patient is a suitable candidate for this study prior to randomization.	____

All responses in above section must be "Yes."

Stratification Factor

Prior 1st line chemotherapy received
 ___ Bevacizumab
 ___ No bevacizumab

Linear Analog Self Assessment value
 ___ ≤ 7
 ___ > 7

Cycles of standard chemotherapy received
 ___ 2-3
 ___ 4-6

Histology
 ___ Predominantly squamous cell
 ___ Not predominantly squamous cell NSCLC

Assigned Treatment

___ A) No Radiation Therapy
 ___ B) Radiation Therapy

Person registering Signature _____ Registration Office specialist initials _____
 Physician Signature _____ Date (mm/dd/yyyy) ___/___/____

PLACE LABEL HERE

NORTH CENTRAL CANCER TREATMENT GROUP

Protocol Number: N0724

Patient ID Number: _____ Patient Initials: _____
L F M

Institution Number: _____

Institution: _____

ON-STUDY FORM

ALL ITEMS MUST BE COMPLETED

Are data amended? (check one) Yes No
 (if data are amended, please circle in red when using paper form)

Description of Primary Disease

MedDRA code: 10029514 [Non-small cell lung cancer, NOS]

Histologic Type (check one)

- 1 Squamous cell (or if mixed, predominantly squamous cell) carcinoma
- 2 Bronchoalveolar carcinoma (BAC)
- 3 Adenocarcinoma
- 4 Non-small cell lung cancer (NSCLC) NOS
- 5 Large cell undifferentiated
- 6 Other, Specify Other Histologic Type: _____

Histologic Grade (Differentiation) (check one)

- 1 Grade I (well)
- 2 Grade II (moderate)
- 3 Grade III (poor)
- 4 Grade IV (undifferentiated, anaplastic)

Status of Primary Tumor (check one)

- 1 Resected with no residual
- 2 Resected with known residual
- 3 Unresected

Disease Status

Method of Evaluation*	Date (mm/dd/yyyy)
<input type="checkbox"/> Primary	____/____/____
<input type="checkbox"/> First Metastasis	____/____/____

* (1=Evaluated but no disease found (can only be used for first Metastasis) 2=Biopsy 3=Cytology 4=Clinical 6=Not evaluated)

Metastatic Site(s) Method of Evaluation*

<input type="checkbox"/> Hilar nodes	<input type="checkbox"/> Bone marrow	<input type="checkbox"/> Adrenal(s)	<input type="checkbox"/> Pleura
<input type="checkbox"/> Ipsilateral Lung	<input type="checkbox"/> Mediastinal nodes	<input type="checkbox"/> Brain	<input type="checkbox"/> Bone
<input type="checkbox"/> Liver	<input type="checkbox"/> Contralateral Lung	<input type="checkbox"/> Supraclavicular/ scalene nodes	<input type="checkbox"/> Skin
			<input type="checkbox"/> Other, specify _____

* (1=Evaluated but no disease found 2=Biopsy 3=Cytology 4=Clinical 6=Not evaluated)

Previous Surgery Related To The Tumor

Surgical Approach	Surgery Results			Date of prior surgery (mm/dd/yyyy)
Mediastinoscopy (check one)	1 <input type="checkbox"/> Positive	2 <input type="checkbox"/> Negative	3 <input type="checkbox"/> Not Done	____/____/____
Bronchoscopy (check one)	1 <input type="checkbox"/> Positive	2 <input type="checkbox"/> Negative	3 <input type="checkbox"/> Not Done	____/____/____
Supraclavicular biopsy (check one)	1 <input type="checkbox"/> Positive	2 <input type="checkbox"/> Negative	3 <input type="checkbox"/> Not Done	____/____/____
Thoracoscopy (check one)	1 <input type="checkbox"/> Positive	2 <input type="checkbox"/> Negative	3 <input type="checkbox"/> Not Done	____/____/____
Fine Needle Aspirate (check one)	1 <input type="checkbox"/> Positive	2 <input type="checkbox"/> Negative	3 <input type="checkbox"/> Not Done	____/____/____
Other, specify (check one)	1 <input type="checkbox"/> Positive	2 <input type="checkbox"/> Negative	3 <input type="checkbox"/> Not Done	____/____/____

PLACE LABEL HERE

NORTH CENTRAL CANCER TREATMENT GROUP

ON-STUDY FORM

ALL ITEMS MUST BE COMPLETED pg 2 of 2

Are data amended? (check one) Yes No
(if data are amended, please circle in red when using paper form)

Protocol Number: N0724
Patient ID Number: _____ Patient Initials: _____
Institution Number: _____ L F M
Institution: _____

Prior Radiation Therapy (other previous malignancies)? (check one) 1 Yes 2 No

If Yes:

Prior RT Site	Total (Dose) cGy Administered	Prior radiation therapy start date (mm/dd/yyyy)	Prior radiation therapy stop date (mm/dd/yyyy)
		__/__/____	__/__/____
		__/__/____	__/__/____
		__/__/____	__/__/____

Prior systemic (cancer) therapy (other previous malignancies) (check one) 1 Yes 2 No

If Yes:

Prior Treatment Name	Prior systemic therapy start date (mm/dd/yyyy)	Prior systemic therapy stop date (mm/dd/yyyy)	Response (NED, CR, PR, REGR, SD, PD)
	__/__/____	__/__/____	
	__/__/____	__/__/____	
	__/__/____	__/__/____	

Has the patient had any prior cancer diagnosed? (check one) 1 Yes 2 No

If Yes: Site of prior cancer: _____
Prior Cancer Diagnosis Date (mm/dd/yyyy) __/__/____
Prior Treatment Regimen Type: _____

Descriptive Factors:

Number of metastatic sites at on-study: (check one) 1 2 3

Response to initial standard chemotherapy: (check one) 2 PR 3 SD

Measurable disease: (check one) 1 Yes 2 No

Brain metastases: (check one) 1 Yes 2 No

Height (cm): _____