RADIATION THERAPY ONCOLOGY GROUP

RTOG 0623

A Phase II Trial Of Combined Modality Therapy With Growth Factor Support

SCHEMA

RTOG Institution # _____

RTOG 0623 **ELIGIBILITY CHECKLIST (1/8/08)**

Case # 10.02 3897.2 690.66 46.8 1.08 refBT/TT2 1 Tf10.02 0 0 10.02 144 692.82 Tm5.1114 Tc0 Tw( )Tj/TT4 1 Tf13.024

_____(Y/N) 17. Did the patient have a prior invasive malignancy (with the exception of non-melanomatous skin cancer or other micro-invasive malignancy)?

_____(Y) If yes, has the patient been disease free for at least three years?

_____(N) 18. Did the patient have previous chemotherapy for lung cancer? (note that prior chemotherapy for a different cancer is allowable if completed ≥ 5 years prior to registration)

_____(N) 19. Did the patient have prior radiotherapy to the region of the study cancer that would result in overlap of radiation therapy fields?

_____(N) 20. Has the patient had weight

early theoretical concerns that growth factors may release progenitor cells and expose them to damage by radiation therapy.[6] Therefore, hematopoietic growth factors have not been recommended during CT/RT, and have not been tested again in this setting despite other significant improvements in supportive care over the last decade. It is, however, conceivable that, in addition to potential differences between the two growth factors (GM-CSF and G-CSF), t

t decade, with the use om 3-D conformal therapy and better defined
erns and allow this issue to be revisited.

n-etoposide combined with accelerated TRT in limited stage small cell
es om grade 3-4 leukopenia among 10
ng 3 episodes om infection. Data on

3.1.2 Patients must have limited disease, i.e., confined to one hemithorax, but excluding T4 tumor based on malignant pleural effusion or N3 disease based on contralateral supraclavicular involvement.

3.1.3 Patients must have measurable or evaluable disease, and location, type, and size of all measurable lesions present prior to treatment must be recorded.

3.1.4 Limited SCLC, including no distant metastases, based upon the following minimum diagnostic workup:

3.1.4.1 History/physical examination (including documentation of recent weight loss, psychiatric history, head injury, or drug/alcohol abuse) within 8 weeks prior to registration;

3.1.4.2 CT scan of chest and upper abdomen, with contrast, within 4 weeks prior to registration; Note: An MRI of the chest is not recommended. PET is permitted in addition to the CT scan but not in place of it.

3.1.4.3 MRI or CT scan of the brain within 4 weeks prior to registration;

3.1.4.4 Radionuclide bone scan (if no PET is done) within 4 weeks prior to registration;

3.1.5 Zubrod Performance Status 0-1(Appendix III);

3.1.6 Age ≥ 18;

3.1.7 CBC/differential obtained within 2 weeks pr

3.1.4.1 NCe)

- Federalwide Assurance (FWA) number;
- For Canadian sites: Health Canada's TPD Forms.

5.2.2 Note: International sites

information is required to assure that mechanisms usually triggered by web registration (e.g., drug shipment, confirmation of registration,

6.3 Localization, Simulation, and Immobilization

6.3.1 A volumetric treatment planning CT study will be required to define gross tumor volume (GTV), clinical target volume (CTV), and planning target volume (PTV) [see definitions below]. Each patient will be positioned in an immobilization device in the treatment position on a flat table. Contiguous CT slices are obtained through the regions harboring gross tumor and grossly enlarged lymph nodes starting from the level of the cricoid cartilage and extending inferiorly through the entire liver volume. 3 mm CT slices should be used through the target volume area.

6.3.2 A treatment planning FDG PET/CT scan (or FDG-PET alone) with the patient in the treatment position is recommended for treatment planning.

6.3.3 Intravenous contrast during the planning CT is optional if a diagnostic chest CT was done with contrast to delineate the major blood vessels. If not, a contrast and a non-contrast CT should be acquired during simulation. The CT scans with and without contrast are registered, and the tumor volumes are contoured on the contrast study, while the non-contrast study is used for dose calculation.

6.3.4 Tumor motion due to respiration must be taken

For use of free-breathing CT for planning, the margin for internal motion should be at least 1.0 cm. An additional set-up margin of at least 0.5 cm should be used for setup uncertainties. The use of fluoroscopy to determine the margin for motion is encouraged.

For **large** field irradiation, PTV1=CTV1 + appropriate margins (as above) is used for planning. For **boost** field irradiation, PTV2=CTV2 + appropriate margins (as above) is used for planning.

6.4.1.5

6.10 Prophylactic Cranial Irradiation (PCI)

6.10.1

- Allergic: Rare anaphylactic-like reactions, sometimes with hypotension.

In the event that ARDS occurs, filgrastim should be discontinued until resolution of ARDS and patients should receive appropriate medical management for this condition.

Allergic-type reactions occurring on initial or subsequent treatment have been reported in <

Additional questions about supply and delivery should be directed to:

13

Among patients experiencing bone pain, approximately 37% of Neulasta®- and 31% of placebo-treated patients utilized non-narcotic analgesics and 10% of Neulasta®- and 9% of placebo-treated patients utilized narcotic analgesics.

In the active-controlled studies, the use of non-narcotic and narcotic analgesics in association with bone pain was similar between Neulasta®- and filgrast

7.6.5 *Storage:* Pegfilgrastim should be stored refrigerated at 2° to 8°C (36° to 46°F); syringes should be kept in their carton to protect from light until time of use. Shaking should be avoided. Before injection, pegfilgrastim may be allowed to reach room temperature for a maximum of 48 hours but should be protected from light. Pegfilgrastim left at room temperature for more than 48 hours should be discarded. Freezing should be avoided; however, if accidentally frozen, pegfilgrastim should be allowed to thaw in the refrigerator before administration. If frozen a second time, pegfilgrastim should be discarded. Pegfilgrastim should be visually inspected for discoloration and particulate matter before administration. Pegfilgrastim should not be administered if discoloration or particulates1e shobserved.

7.6.6 *Supply:* Commercially available; the use of drug(s) or combination of drugs in this protocol meet the criteria described under Title 21 CFR 312.2(b) for IND exemption.

7.7 Accountability

Drug accountability records must be maintained at all sites1ccording to good clinical practices and NCI guidelines.

7.8 Dose Modifications for Cisplatin and Etoposide

Note: Dose modifications for filgrastim and pegfi
___ allowed unless discussed with the Principal Investigator, Dr. Lilenbaum.

7.8.1 *Definition of Dose Levels of Cisplatin and Etoposide*

Drug	-	2	t	**Dose Level/m**
				2

7.10.2 <u>Serious Adverse Events (SAEs)</u> — All SAEs that fit any one of the criteria in the SAE definition below must be reported via AdEERS within 24 hours of discovery of the event. For medical issues regarding AdEERS, please contact the study Data Manager. For technical and policy related issues regarding AdEERS, please contact the AdEERS Coordinators by email at AdEERSMD@tech-res.com <mailto:AdEERSMD@tech-res.com> or telephone (301) 897-7497.

Definition of an SAE: Any adverse drug experience occurring at any dose that results in any of the following outcomes:

- Death;
- A life-threatening adverse drug experience;
- Inpatient hospitalization or prolongation of existing hospitalization;
- A persistent or significant disability/incapacity;
- A congenital anomaly/birth defect.

Important medical events that may not result in death, be life threatening, or require [illegible] may

9.0 OTHER THERAPY

9.1 Permitted Supportive Therapy

9.1.2 All supportive therapy for optimal medical care will be given during the study period at the discretion of the attending physician(s) within the parameters of the protocol and documented on each site's source documents as concomitant medication.

9.2 Non-permitted Supportive Therapy

9.2.1 Administration of amifostine (Ethyol®) is not permitted on this study.

10.0 TISSUE/SPECIMEN SUBMISSION

Not applicable to this study.

11.0 PATIENT ASSESSMENTS

11.1 Study Parameters: See Appendix II for a summary of assessments and time frames.

11.2 Evaluation During Study

11.2.1 If clinically indicated, urinalysis with microscopy should be done prior to starting the first cycle of chemotherapy.

11.2.2

Clinical lesions: Clinical lesions will only be considered measurable when they are superficial (e.g., skin nodules and palpable lymph nodes). In the case of skin lesions, documentation by color photography, including a ruler to estimate the size of the lesion, is recommended.

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11.5 Criteria for Discontinuation of Protocol Treatment

The sample size was calculated using the method of Fleming

13.4 Analysis Plans

13.4.8 This study will be monitored by the Clinical Data Update System (CDUS) version 3.0. Cumulative CDUS data will be submitted quarterly by electronic means. Reports are due January 31, April 30, July 31, and October 31.

13.5 Gender and Minorities

Ciampi, et al.[16] performed a recursive partitioning analysis on small cell lung cancer dataset and found that gender does influence overall survival in limited stage patients. This has not been shown to be consistent by 4sisIthorts.Ine corforl

Study Plan

Another way to find out what will happen to you during the study is to read the chart below. Start reading at the top and read down the list, following the lines and arrows.

What side effects or risks can I expect from being in the 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, researchers 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 radiation treatment, chemotherapy, and/or filgrastim/pegfilgrastim. In some cases, side effects can be serious, long lasting, or may never go away. There also is a risk of death.

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

Risks Associated With Radiation to the Chest

Very Likely

- Difficulty, pain, or burning sensation when swallowing, which is temporary; the use of chemotherapy with radiation may increase this risk. You should avoid acidic or spicy foods and alcoholic beverages.
- on, Fatigue (tiredness) temporary
- Hair loss in the area

may become reddened and/or dry, and chest hair may not grow back

nts while undergoing treatment, which could lead to an increased risk of infection,

eeding and bruising easily

ng, due to lung damage, as described below

- Irritation of the lining around the heart, which can caus

- Low magnesium in the body
- Low calcium in the body (It is unlikely that the

Who can answer my questions about the study?

You can talk to your study doctor about

APPENDIX II: STUDY PARAMETER TABLE

APPENDIX III

ZUBROD PERFORMANCE SCALE

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APPENDIX IV

APPENDIX IV (Continued)

AJCC Staging
Lung, 6th Edition, 2002

Distant Metastasis (M)

MX Distant metastasis cannot be assessed
M0 No distant metastasis
M1 Distant metastasis present

Note:

APPENDIX V

RTOG 0623, Study Agent Shipment

Filgrastim will be shippef2 1