RTOG 0320, “A PHASE III TRIAL COMPARING WHOLE BRAIN RADIATION AND STEREOTACTIC RADIOSURGERY ALONE VERSUS WITH TEMOZOLOMIDE OR ERLOTINIB IN PATIENTS WITH NON-SMALL LUNG CANCER AND 1-3 BRAIN METASTASES”

Study Chair: Paul W. Sperduto, MD, MAPP; 952-442-6000; psperduto@mropa.com

RTOG 0320 has been amended as follows:
As mandated by CTEP, beginning October 1, 2011, this study will utilize CTCAE version 4.0 for AdEERS reporting of adverse events. Related changes were made to Section 6.81 and 7.6.

NOTE: All AE reporting on the study case report forms will continue to use CTCAE version 3.0.

Cover Page: A document version history was added to the Cover Page per current RTOG standard. Contact information was updated for Dr. Wang and Dr. Mehta.

Global: All currently necessary weblinks to sub-pages of the RTOG website were updated.
SUMMARY OF CHANGES
Amendment # 7, Version Date: 4/24/09
(Broadcast Date: 5/28/09)

RTOG 0320, "A PHASE III TRIAL COMPARING WHOLE BRAIN RADIATION AND STEREOTACTIC RADIOSURGERY ALONE VERSUS WITH TEMOZOLOMIDE OR ERLOTINIB IN PATIENTS WITH NON-SMALL LUNG CANCER AND 1-3 BRAIN METASTASES"

Study Chair: Paul W. Sperduto, MD, MAPP; 952-442-6000; psperduto@mropa.com

In response to a CTEP Request for Rapid Amendment (RRA), RTOG 0320 was amended to reflect changes to the Comprehensive Adverse Events and Potential Risks List (CAEPR) for erlotinib. Changes were made to the following sections:

Section 7.2.7.3: The 4th to last paragraph ("The use of drugs that alter gastric pH (e.g. proton pump inhibitors and H2 antagonists) may interfere with the absorption of erlotinib. As a result, these drugs should be administered at least 4 hours after erlotinib administration.")) was replaced with the paragraphs headed "Proton Pump Inhibitors" and "H2-antagonist."

Section 7.2.8:

- The paragraphs headed "Gastrointestinal Perforation," "Bullous and Exfoliative Skin Disorders," and "Ocular Disorders" were added.
- In Table 2, Dose Reduction Criteria and Guidelines for Management of Erlotinib Related Adverse Events, the last 2 rows were added (GI/bowel perforation and ocular adverse events).

Section 7.2.9: Erlotinib CAEPR Version 2.1 (September 18, 2008) was replaced by CAEPR Version 2.2 (April 7, 2009). Specific changes are as follows:

- Added new risk
  - Less likely: Ocular/visual - Other (Eyelash in-growth or thickening)
  - Rare but serious: Ocular/visual - Other (Corneal perforation)
  - Reported on erlotinib trials but with the relationship to erlotinib still undetermined: Adult Respiratory Distress Syndrome (ARDS); Cholecystitis; Colitis; DIC (disseminated intravascular coagulation); Esophagitis; Gastitis (including reflux gastritis); Pain - Throat/pharynx/larynx; Urticaria (hives, welts, wheals)

- Deleted risk
  - Less likely: Pain - Oral cavity
  - Reported on erlotinib trials but with the relationship to erlotinib still undetermined: Anxiety; Fever; Joint pain (arthralgia); Mucosal
inflammation; Muscle pain (myalgia); Neutropenia; Pulmonary fibrosis; Weight loss

- **Increase in risk attribution**
  - *Changed to less likely from rare but serious*: Pneumonitis/pulmonary infiltrates
  - *Changed to less likely from reported but undetermined*: Dehydration; Hemorrhage, GI - Select; Infection (documented clinically or microbiologically) with Grade 3 or 4 neutrophils (ANC <1.0 x 10^9/L) - Select
  - *Changed to rare but serious from reported but undetermined*: Hemorrhage, CNS; Keratitis (corneal inflammation/corneal ulceration); Perforation, GI - Select

- **Decrease in risk attribution**
  - *Changed to less likely from likely*: Nausea

- **Modified Agent Specific Adverse Events List (ASAEL) reporting requirements**
  - *Added*: Cough; Dehydration; Dyspnea (shortness of breath); Ocular surface disease; Pain - Abdomen NOS *Deleted*: Rash: hand-foot skin reaction

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**Section 9.7.9: Added**

**Appendix I, Informed Consent**: The risk profile for erlotinib was replaced with CTEP's revised risk profile corresponding with the updated CAEPR.

*The following editorial/administrative change was also made:*

**Section 7.2.10**: The spelling of erlotinib was corrected in the 2nd-to-last sentence.
SUMMARY OF CHANGES
Amendment # 6, Version Date: October 15, 2008
(Broadcast Date: October 27, 2008)

RTOG 0320, "A PHASE III TRIAL COMPARING WHOLE BRAIN RADIATION AND STEREOTACTIC RADIOSURGERY ALONE VERSUS WITH TEMOZOLOMIDE OR ERLOTINIB IN PATIENTS WITH NON-SMALL LUNG CANCER AND 1-3 BRAIN METASTASES"

Study Chair: Paul W. Sperduto, MD, MAPP; 952-442-6000; psperduto@mropa.com

In response to an NCI Special Request for a Rapid Protocol Amendment from Helen Chen, MD, RTOG 0320 was amended as follows to reflect changes to the CAEPR for erlotinib, including dose modification guidelines and risk sections of the informed consent:

Section 3.1.9: "Total bilirubin: within normal institutional limits" was added to this section for consistency with NCI's protocol template for erlotinib regarding liver function tests; "all" was changed to "other" regarding liver function tests. "< 2 x institutional upper limit of normal (uln)" remains as stated in the protocol because that criterion is more stringent than that of the NCI's protocol template for erlotinib.

Section 7.2.8: In Table 2, dose modification guidelines for erlotinib, the stipulations have been further clarified to advise interruption or discontinuation of erlotinib for Grade 3-4 liver function abnormalities.

Section 7.2.9: The existing CAEPR for erlotinib was replaced with the newly revised CAEPR, Version 2.1, September 18, 2008.

Appendix I, Informed Consent: Under "Risks Associated with Erlotinib," the following changes were made:

- "Tiredness" and "vomiting" were moved from "Less Likely" to "Likely"
- "Loss of appetite" was added to "Likely" and "Decreased appetite" was removed from "Less Likely"
- "Dry skin" and "itching" were moved from "Likely" to "Less Likely"
- "Fever" was deleted from "Less Likely" because this is reported but undetermined.
- "Nail changes" and "sore mouth" were added to "Less Likely"
- Risks of "abnormal liver enzymes" appearing in the new version of the CAEPR already appear under "Less Likely"
- Under "Rare But Serious" the following were added:
- Blistering and sloughing of the skin or gut lining which can be life-threatening
- Painful redness or peeling of the skin on the palms of the hands and soles of the feet
- Liver failure that can be life-threatening or fatal, particularly in patients with underlying impairment of the liver function

The following text was added to the end of the section: "Side effects may be mild or very serious. Many side effects go away soon after you stop taking erlotinib. In some cases, side effects may be long lasting or may never go away. There also is a risk of death."
SUMMARY OF CHANGES
Amendment # 5, Version Date: July 22, 2008
(Broadcast Date: October 14, 2008)

RTOG 0320, "A PHASE III TRIAL COMPARING WHOLE BRAIN RADIATION AND STEREOTACTIC RADIOSURGERY ALONE VERSUS WITH TEMOZOLOMIDE OR ERLOTINIB IN PATIENTS WITH NON-SMALL LUNG CANCER AND 1-3 BRAIN METASTASES"

Study Chair: Paul W. Sperduto, MD, MAPP; 952-442-6000; psperduto@mropa.com

RTOG 0320 was amended as follows:

Title Page: The statistician's name and contact number were added.

Eligibility Checklist: The first sentence of the last paragraph "calling RTOG" was changed to "web registration."

Section 5.1: This section was amended to reflect the most current RTOG pre-registration procedures.

Section 5.2.1: This section was amended for clarity and the web link for Human Subjects Training was updated.

Sections 6.8 and 7.6: These sections were amended to reflect the most current Adverse Event Reporting Guidelines. In addition, "MedDRA 6.0" was added to the first sentence in 7.6.

Section 7.1.7.2: A new third paragraph was added. In the fourth paragraph, the first sentence was changed to include international shipments and "after registration of the patient" was added to the end of the second sentence. The contact information for I.V. Solutions was updated.

Section 9.3.2: The fourth sentence in this section, which referred to a minimum of 2 post-XRT cycles of temozolomide was removed because per Amendment #4, it is no longer a requirement.

Section 13.7: The heading was revised.

Appendix I, Consent: At the request of the CIRB, the following changes were made

- Under "Risks Associated with Temozolomide": "death" was added under "Rare But Serious" and two paragraphs were added to include the risk of the development of secondary malignancies;
• Under "What Are My Rights as a Participant," the first paragraph was replaced with a new one.

Appendix IV: Instructions for the Study Agent Shipment Form have replaced the actual form, which is posted on the RTOG website.
SUMMARY OF CHANGES
Amendment # 4, Version Date: May 8, 2007

RTOG 0320, "A PHASE III TRIAL COMPARING WHOLE BRAIN RADIATION AND STEREOTACTIC RADIOSURGERY ALONE VERSUS WITH TEMOZOLOMIDE OR ERLOTINIB IN PATIENTS WITH NON-SMALL LUNG CANCER AND 1-3 BRAIN METASTASES"

Study Chair: Paul W. Sperduto, MD, MAPP; 952-442-6000; psperduto@mropa.com

RTOG 0320 chemotherapy options allowed after WBRT have been amended as follows:

Schema: For Arm 2, the text was revised as: "After WBRT, temozolomide may be discontinued at investigator's discretion or continued. If continued, then four weeks after the completion of WBRT, 150mg/m²/day for 5 days/month if prior or concurrent chemotherapy (200mg/m²/day for 5 days/month if no prior chemotherapy) until progression (systemic or CNS) or for a maximum of 6 additional cycles or until the drug is discontinued at the investigator's discretion." For Arm 3, the text was revised as: "After WBRT, the erlotinib may be discontinued at investigator's discretion or continued. If continued, it will continue for a maximum of 6 months after completion of WBRT + SRS."

Section 3.1.4: "Patients who present with synchronous brain metastases at the time of the initial diagnosis of lung cancer are eligible" was added for clarity.

Section 3.1.9: The following text was added to the end of the section for clarity: If the liver function tests, specifically the alkaline phosphatase is elevated above the allowed limit, but this is deemed to be due to bone metastases and not liver metastases, the patient is eligible.

Section 7.1.8.3: A new first sentence was added describing the options after WBRT. A new second paragraph was added for patients who present with synchronous brain metastasis(es) and systemic disease. The end of the fourth sentence was amended as "until progression or for a maximum of 6 additional cycles or until the drug is discontinued at the investigator's discretion."

Section 7.1.8.4: The original section was deleted as this information was incorporated into Section 7.1.8.3. As a result, subsequent Sections 7.1.8.5 and 7.1.8.6 were renumbered as 7.1.8.4 and 7.1.8.5. Cross REFERENCES to these sections within the text were renumbered.

Section 7.1.9: A new first bullet was added. Under the fifth bullet, "After completion of 2 cycles of temozolomide" was deleted for consistency with the other changes to the protocol.
Section 7.2.7.2: The second part of the third sentence was changed to "or erlotinib may be discontinued after the whole brain radiation therapy at the investigator's discretion."

Section 9.3.2: The last sentence of the third paragraph was deleted. A new fourth paragraph was added for patients who present with synchronous brain metastasis(es) and systemic disease.

Section 9.3.3: This section was amended for consistency with the rest of the protocol to indicate that there is an option after WBRT of discontinuing erlotinib at the investigator's discretion.

Consent:

- Under "What Is Involved In The Study," under "Definitions," additional text was added to temozolomide and erlotinib for consistency with changes made to the protocol.
- Under Risks Associated with Temozolomide, a new last paragraph was added at the request of the CIRB.
- Under Risks Associated with Erlotinib, under the first bullet, "on the" was added before "face."
SUMMARY OF CHANGES

Amendment # 3, Version Date: April 6, 2006

RTOG 0320, "A PHASE III TRIAL COMPARING WHOLE BRAIN RADIATION AND STEREOTACTIC RADIOSURGERY ALONE VERSUS WITH TEMOZOLOMIDE OR ERLOTINIB IN PATIENTS WITH NON-SMALL LUNG CANCER AND 1-3 BRAIN METASTASES"

Study Chair: Paul W. Sperduto, MD, MAPP; 952-442-6000; psperduto@mropa.com

RTOG 0320 has been amended as follows:

Eligibility Checklist: Question # 12 was reworded to eliminate reference to original Section 3.1.9 and now refers only to renumbered Section 3.1.9. Question # 16 was reworded for consistency with the change made to Section 3.2.8. Question # 23 was added to correspond with new Section 3.2.16.

Section 3.1.9 (old): This section was deleted as contrast-enhancing CT scans of the chest, abdomen and pelvis, and bone scan are no longer required for eligibility. The subsequent sub-sections of Section 3.1 were renumbered. As a result of the deletion of 3.1.9, corresponding assessments were deleted from Section 11.1. These changes were made because a patient may not have disease in areas for which scans were mandated; treating physicians have the best insight into which scans may or may not be appropriate for any given patient. A new Section 4.3 was added.

Section 3.2.8: The wording of this section was changed to: "Patients with known or pre-existing liver metastases."

Section 3.2.16: This new section was added to exclude patients with previous temozolomide or erlotinib.

Section 7.1.7: The last sentence was deleted at the request of the pharmaceutical company.

Section 7.1.8.5: In the first sentence of the third paragraph, three weeks was changed to two weeks for consistency with the rest of the protocol.

Section 7.1.8.6: In the table for "Dose Reduction Schedule-Cycle 1," under "Regimen/Day," "x 2 weeks" was deleted to avoid confusion.

Section 7.1.8.6.1: In second sentence of the last paragraph, 125 mg/m²/day was corrected to 100 mg/m²/day.
**Section 7.2.8:** Under (c), in the first sentence, 3 weeks was changed to 2 weeks for consistency with the rest of the protocol.

**Section 11.1:** A new footnote "e" was added to "CBC differential, platelets" under the column "Monthly During Protocol Drug Treatment" to define the appropriate frequency of blood counts to assure patient safety.

**Consent:** Under What Is Involved In the Study, the schedule for Blood Counts, Chemistries was amended as "Prior to study entry, during drug treatment and after the radiation treatment period" to reflect the changes made to the text of the protocol. "Chest, Abdomen, Pelvic CT Scan, and Bone Scan" procedures were deleted as they were from the protocol.
SUMMARY OF CHANGES

Update Date: September 23, 2005

RTOG 0320, “A PHASE III TRIAL COMPARING WHOLE BRAIN RADIATION AND STEREOTACTIC RADIOSURGERY ALONE VERSUS WITH TEMOZOLOMIDE OR ERLOTINIB IN PATIENTS WITH NON-SMALL LUNG CANCER AND 1-3 BRAIN METASTASES”

Study Chair: Paul W. Sperduto, MD, MAPP; 952-442-6000; psperduto@mropa.com

RTOG 0320 has been updated as follows:

Section 6.8: The first bullet in the table was changed to 10 days (from 5 days) to match the body of the table.

Section 11.1: For clarity, BrCS, LCS, EQ-5D was deleted at “Pre-SRS Wk 4”; under “Every 6 Months Thereafter,” “18 & 24 months only” was added; in footnote “a,” “Pre-SRS (week 4)” was deleted; and under “Definitions” in the consent, “at week 4” was deleted from Quality of life Questionnaires.

Consent: In the second bullet, under “Rare, but Serious” risks of erlotinib, “OSI” was changed to “erlotinib” for patient clarity.
RTOG 0320, “A PHASE III TRIAL COMPARING WHOLE BRAIN RADIATION AND STEREOTACTIC RADIOSURGERY ALONE VERSUS WITH TEMOZOLOMIDE OR ERLOTINIB IN PATIENTS WITH NON-SMALL LUNG CANCER AND 1-3 BRAIN METASTASES”

Study Chair: Paul W. Sperduto, MD, MAPP; 952-442-6000; psperduto@mropa.com

RTOG 0320 has been amended as follows to incorporate the revised NCI Adverse Events Reporting Guidelines, version 2.0 of the CAEPR for OSI-774, and the Informed Consent Modification required by the CIRB:

Section 6.8: This section was rewritten in order to incorporate the AdEERS radiation therapy (RT)-only pathway for reporting of radiation adverse events experienced on the RT-only arm of the study.

Section 7.2.9: Version 2.0 of the Comprehensive Adverse Events and Potential Risks (CAEPR) for OSI-774 replaced version 1.0 of the CAEPR for OSI-774 as required by NCI.

Section 7.6: As required by NCI, this section was rewritten in accordance with the revised NCI Adverse Events Reporting Guidelines.

Section 7.7: As required by NCI, a new section, “AdEERS Expedited Reporting Requirements,” was added to conform to the revised NCI Adverse Events Reporting Guidelines.

Section 13.6: The Clinical Data Update System (CDUS) was updated from version 1.1 to the current version 3.0 in the first sentence.

Consent:

- Under “Risks Associated with Temozolomide,” the language in the second bullet under “Likely,” was deleted and replaced by three new bulleted risks as required by the NCI Central IRB Initiative (CIRB).
- Under “Risks Associated with Erlotinib,” under “Likely,” tiredness, acne, and dry mouth were deleted and under “Less Likely,” tiredness, acne, dry mouth, fever, cough were added for consistency with the updated CAEPR for OSI-774 in Section 7.2.9.
The section “Risks of Antibiotic Treatment to Prevent Pneumocystis Pneumonia” was taken out in order to simplify the consent and avoid patient confusion as this treatment is not a study requirement. At the end of the section, “Risks Associated with Temozolomide,” the following text was added: “Because there is a risk of contracting a type of pneumonia called pneumocystis pneumonia when you are receiving temozolomide at the same time as radiation therapy to the brain, you may receive a preventive medicine.”

Appendix IV: The study agent shipment form was revised for clarity. The second paragraph of Section 5.1 was amended to correspond with the instructions on the study agent shipment form and in Section 7.1.7.2.
SUMMARY OF CHANGES

Amendment # 1, Version Date: May 3, 2005

RTOG 0320, “A PHASE III TRIAL COMPARING WHOLE BRAIN RADIATION AND STEREOTACTIC RADIOSURGERY ALONE VERSUS WITH TEMOZOLOMIDE OR ERLOTINIB IN PATIENTS WITH NON-SMALL LUNG CANCER AND 1-3 BRAIN METASTASES”

Study Chair: Paul W. Sperduto, MD, MAPP; 952-442-6000; psperduto@mropa.com

RTOG 0320 has been amended to replace gefitinib with erlotinib as follows:

Title Page, Schema, Appendix I, Appendix IV: “Gefitinib” was replaced with “Erlotinib” in the title of the protocol.

Index, Appendix VII: The “Iressa” in the title of Appendix VII was changed to “Erlotinib.”

Schema: Arm 3 was changed to “WBRT + SRS + Erlotinib” on the schematic. Under Arm 2, “brain” was changed to “CNS” for consistency with the rest of the protocol. Under Arm 3, the text was changed to: “WBRT + SRS + Erlotinib 150mg/day daily beginning on day 1 of WBRT and continuing up to progression (CNS) or a maximum of 6 months after completion of WBRT + SRS.”

Eligibility Checklist: Question # 22 was added to page 1 to be consistent with new Section 3.2.15.

Section 1.1, 1.9, 2.1, 3.1.11, 7.1.9 fourth bullet, 9.3, 9.4, 9.7.3, 12.1, 13.2.1: Erlotinib replaced gefitinib.

Section 1.6.4: In the 3rd paragraph, reference 78 was deleted. There were new references added necessitating the renumbering of references from this point forward throughout the protocol text and list of References.

Section 1.7: This was entirely revised for erlotinib. The information pertaining to gefitinib was eliminated.

Section 2.2: In the last sentence, “and” was deleted before “cause” and “and effects of non-protocol chemotherapy” was added to the end.

Section 3.2.15: “History of allergic reactions attributed to compounds of similar chemical or biologic composition to erlotinib and temozolomide” was added as an ineligibility.
Section 5.2: This section was rewritten to provide instructions for web registration.

Section 7.1.7.2: In the first sentence, “patient-specific drug supply” was replaced with “temozolomide” and the 2nd sentence in the 3rd paragraph was changed to “Canadian shipments may require additional time” for clarification. A new 4th paragraph was added with additional instructions.

Section 7.2: This section was heavily revised to incorporate drug information for erlotinib. The information pertaining to gefitinib was deleted.

Section 7.2.2: In the second sentence, “Genentech” was replaced with “OSI Pharmaceuticals, Inc.”

Section 7.2.7.3: “Grapefruit juice may change the level of erlotinib in the blood. Therefore, patients must be advised to avoid grapefruit while taking erlotinib” was added at the end of the section.

Section 7.3: In the Clinical Trials Agreement, “erlotinib” and “OSI Pharmaceuticals, Inc.” replaced “gefitinib” and “AstraZeneca.”

Section 9.4.2: In the second sentence, “provided below” was deleted.

Section 9.7.4: The following was added: “Previous trials have shown that the frequency and severity of diarrhea rarely hindered administration of erlotinib and could be managed with loperamide. The recommended dose is loperamide 4 mg at first onset, followed by 2 mg q 2–4 hours until diarrhea free for 12 hours.”

Section 9.7.8: This section on antibiotics was added.

Section 13.1.2: “Effects of non-protocol chemotherapy” was added to the Secondary Endpoints.

Section 13.2.1: In the first paragraph, last sentence, 5.8 was changed to 5.9 months.

Section 13.2.2.3: In the third sentence, 5.8 was changed to 5.9 months.

Section 13.2.2.5: In the second paragraph, first sentence, 5.8 was changed to 5.9 months.

Section 13.2.2.7: This new section “Effects of non-protocol chemotherapy” was added.

Appendix I: The following changes were made in the sample consent:

- In the first paragraph, “study” was added to “doctor” in the last sentence.
Under “Why Is This Study Being Done,” erlotinib replaced gefitinib in the last sentence of the first paragraph.

Under “What Is Involved In The Study,” erlotinib replaced gefitinib in # 3, under Definitions, “Temozolomide should be taken with water on an empty stomach. It is best to take it at bedtime” was added for temozolomide, “Erlotinib should be taken with water preferably in the morning 1 hour before or 2 hours after food” was added for erlotinib; in the fourth paragraph concerning warfarin, and in the last paragraph as a drug being tested in this study, where it now states that “Erlotinib is FDA approved for the 2nd line treatment (the most effective treatment after the first treatment has failed) of NSCLC (Non-Small Cell Lung Cancer)”. The last sentence of the section was revised as: “Both drugs have been used in patients with central nervous system tumors and preliminary evidence suggests they may be of benefit.”

Under “Risks Associated with Whole Brain Radiation Therapy” erlotinib replaced gefitinib in the first sentence.

At the end of the section, “Risks Associated with Temozolomide,” “Temozolomide capsules should not be opened.” was added.

Risks Associated with Erlotinib” replaced “Risks Associated with Gefitinib.”

- Under Likely, “If eye irritation develops while wearing contact lenses, stop wearing them immediately and seek medical attention” was added to the risk of “Inflammation of the eye.”
- Under Less Likely, “Sleepiness” was replaced with “Cannot sleep”; “Rapid Heartbeat” was changed to “Slow heartbeat”; “or low platelet count (which leads to bleeding)” was added to “Decreased red cell levels”; “Abnormal kidney function test results that may indicate problems with your kidney” was deleted; and “gefitinib” was replaced with “erlotinib” in the last paragraph.
- Under Rare, But Serious, “gefitinib” was replaced by “erlotinib” in the first sentence; “Gefitinib has caused small changes in the electrical activity of the heart in a few animals, but this has not occurred in people” was deleted at the beginning of the bullets; in the first bullet “gefitinib” was replaced with “erlotinib” and “study” was added to doctor in two places; seven new bullets (risks) were added; in the last sentence “gefitinib” was replaced with “erlotinib”; the prior last sentence concerning grapefruit juice was deleted.
- A new section, “Drugs that interfere with the activity of erlotinib” was added after “Risks Associated with Erlotinib.”
- Under “Reproductive Risks,” a new third sentence was added to the third paragraph.
- Under “Are There Benefits To Taking Part in the Study,” in the second paragraph, “gefitinib” was replaced with “erlotinib.”
- Under “What Are The Costs,” “gefitinib” was replaced by “erlotinib” in the second paragraph.
- Under “What Re My Rights As A Participant,” “study” was added to “doctor” in the second sentence.

**Appendix IV:** A line for an Email address was added.

**Appendix VII:** The spelling of “Rifampicin” and “St. John’s Wort” were corrected.
SUMMARY OF CHANGES

Update Date: October 6, 2004

RTOG 0320, “A PHASE III TRIAL COMPARING WHOLE BRAIN RADIATION AND STEREOTACTIC RADIOSURGERY ALONE VERSUS WITH TEMOZOLOMIDE OR GEFITINIB IN PATIENTS WITH NON-SMALL LUNG CANCER AND 1-3 BRAIN METASTASES”

Study Chair: Paul W. Sperduto, MD, MAPP; 952-442-6000; psperduto@mropa.com

RTOG 0320 has been updated as follows:

Section 7.1.7.2: “SPRI” was replaced with “Integrated Therapeutics Group, Inc., a subsidiary of Schering-Plough.”

Section 12.1: Adverse Event Form (AE) due “As applicable for toxicity assessment reporting” was added.

NOTE: These are editorial/administrative changes to the protocol. NCI now requires that these changes be documented on the protocol title page with the date of the update noted as “Update Date”, not as a revision.

An updated protocol is available (no password required) on the RTOG website: www.rtog.org