SUMMARY OF CHANGES
Amendment 6, Version Date: May 6, 2010
(Broadcast 5/13/10)

RTOG 0324, "Phase II Study Of Cetuximab (C225) In Combination With Chemoradiation In Patients With Stage IIIA/B Non-Small Cell Lung Cancer (NSCLC)"

Study Chair: George Blumenschein, M.D., (713) 792-6363, gblumens@mdanderson.org

RTOG 0324 has been amended as follows:

Patient follow up has been amended to the current RTOG standard of the patient's lifetime, and sites are asked to perform annual follow-up evaluations. The following sections were amended for this change: 11.1, 11.2, 12.1 (the schedule for the Follow-up Form), and Appendix I (under "What is involved in the study?" and "How long will I be in the study?").

Other Changes

Title page: Dr. Curran's affiliation and contact information were updated, and the Senior Statistician's contact information was added.

Section 6.12: The heading was amended to current RTOG standard, and the text was replaced with a reference to Section 7.8.

Section 7.5.3.1: In the 2nd to last row of the table, a reference to Section 7.7 was amended to Section 7.8 to be consistent with changes in Sections 7.7 and 7.8.

Section 7.7, "Adverse Events", was added to amend the protocol to current RTOG standards. In addition, the subsequent section, was renumbered to Section 7.8, and the heading and text were amended to current RTOG standards for AdEERS reporting.
RTOG 0324, "Phase II Study Of Cetuximab (C225) In Combination With Chemoradiation In Patients With Stage IIIA/B Non-Small Cell Lung Cancer (NSCLC)"

Study Chair: George Blumenschein, M.D., (713) 792-6363, gblumens@mdanderson.org

---

RTOG 0324 has been amended as follows:

Bristol-Myers Squibb (BMS) has requested that updated information be added to studies involving cetuximab and radiation treatment.

Information about cetuximab pharmacokinetics was added to Section 1.2.2.3 (one sentence at the beginning and one sentence at the end of the third paragraph).

In addition, information regarding clinical studies of cetuximab in head and neck cancer, safety of cetuximab in head and neck cancer clinical trials, and late radiation toxicity was added as Sections 1.3, 1.3.1, 1.3.2, 1.4, and 1.4.1. Subsequent sections were appropriately renumbered (as Sections 1.5 and 1.6.)

Other Changes

Title page: The 800 number for RTOG Headquarters was added.

Section 10.1.3: The phone, fax, and e-mail address for the RTOG Tissue Bank was updated.
RTOG 0324, “Phase II Study Of Cetuximab (C225) In Combination With Chemoradiation In Patients With Stage IIIA/B Non-Small Cell Lung Cancer (NSCLC)”

Study Chair: George Blumenschein, M.D., (713) 792-6363, gblumens@mdanderson.org

RTOG 0324 has been amended as follows:

In a recent Action Letter regarding the occurrence of hypomagnesemia in clinical trials with C225 (cetuximab), NCI mandated that serum magnesium monitoring be added to routine electrolyte monitoring. The monitoring of electrolytes and magnesium was added in the table in Section 11.1. The study chairs also reviewed the risks associated with cetuximab described in Appendix I, as mandated in NCI’s Action Letter, and determined that no additions/changes were necessary at this time.

Other Changes

Title page: Dr. Komaki’s contact information was updated.

Section 5.1.3: The fax number for RTOG Headquarters was corrected.
RTOG 0324, “Phase II Study Of Cetuximab (C225) In Combination With Chemoradiation In Patients With Stage IIIA/B Non-Small Cell Lung Cancer (NSCLC)”

Study Chair: George Blumenschein, M.D., (713) 792-6363, Harari@humonc.wisc.edu

RTOG 0324 has been amended as follows:

A pre-treatment PET scan, rather than a bone scan, is permitted to rule out bone metastases. Sections 3.1.11, 11.1 (footnote “m”), and Appendix I were amended accordingly.

An amended protocol is available (no password required) on the RTOG Web site, http://www.rtog.org
SUMMARY OF CHANGES
Revision 2, Version Date: July 26, 2004

RTOG 0324, “Phase II Study Of Cetuximab (C225) In Combination With Chemoradiation In Patients With Stage IIIA/B Non-Small Cell Lung Cancer (NSCLC)”

Study Chair: George Blumenschein, M.D., (713) 792-6363, Harari@humonc.wisc.edu

RTOG 0324 has been revised as follows:

Title page: The 800 number for RTOG Headquarters was deleted, as this number is not current. The number also was deleted in the tables in Section 7.7.4.

Eligibility Checklist, page 1: Question 20 was corrected to correspond to Section 3.2.11.

Section 3.1.11: For consistency with the schedules of other pretreatment evaluations, the timeframe for FEV1, CT/MRI of the chest and brain, EKG, and bone scan was revised from “28 days prior to the start of protocol treatment” to “4 weeks prior to study entry”. Section 11.1, footnotes “a” and “c” were revised to correspond.

Section 3.2.14, excluding patients who currently are participating in other clinical trials and/or who have participated in other clinical trials in the previous 30 days, was added.

Sections 5.1.2: The RTOG Headquarters address was updated. The address also was updated in Section 12.0.

Section 7.1.2: In the second paragraph, the parenthetical description of RT was deleted.

Section 10.1.3: The email address for LDS Hospital was updated.

Section 11.1:

- Footnote “g” was revised to read, “Recommended every 6 months for 2 years, then annually”;
- Footnote “k” was deleted, and subsequent footnotes were appropriately re-lettered.

Section 12.1: The phrase, “if these events occur between planned follow-up intervals”, was added to the last sentence in the timeframe for the Follow-up Form (F1).

Appendix I, the sample consent:

- In the tests and procedures listed under “What Is Involved In The Study?”, the schedules for tests of lung function and CT/MRI of the chest were corrected to be consistent with Section 11.1.
Under “What Are The Costs”, the last paragraph was deleted, as it was incorrect.

Appendix IV: The shipment form was deleted, and the web address for the updated form was provided.

A revised protocol is available (no password required) on the RTOG Web site, http://www.rtog.org
RTOG 0324, “Phase II Study Of Cetuximab (C225) In Combination With Chemoradiation In Patients With Stage IIIA/B Non-Small Cell Lung Cancer (NSCLC)”

Study Chair: George Blumenschein, M.D., (713) 792-6363, Harari@humonc.wisc.edu

RTOG 0324 has been revised as follows:

The MUGA scan or echocardiogram prior to and at the end of treatment are no longer required. Sections 3.1.11, 11.1, and Appendix I, the sample consent, were revised to reflect this change.

The email address for submission of the initial Cetuximab shipment form was updated in Sections 5.1.3, 7.2.7, and in Appendix IV.

A revised protocol is available (no password required) on the RTOG Web site, http://www.rtog.org
SUMMARY OF CHANGES
Update, April 9, 2004

RTOG 0324, “Phase II Study Of Cetuximab (C225) In Combination With Chemoradiation In Patients With Stage IIIA/B Non-Small Cell Lung Cancer (NSCLC)”

Study Chair: George Blumenschein, M.D., (713) 792-6363, Harari@humonc.wisc.edu

RTOG 0324 has been updated as follows:

Appendix IV — The Clinical Supply Shipment Request form has been updated to correct typo in RTOG fax number, which is 215-574-0300.

NOTE: This is an editorial/administrative change 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: http://www.rtog.org/
SUMMARY OF CHANGES  
Update, April 2, 2004

RTOG 0324, “Phase II Study Of Cetuximab (C225) In Combination With Chemoradiation In Patients With Stage IIIA/B Non-Small Cell Lung Cancer (NSCLC)”

Study Chair: George Blumenschein, M.D., (713) 792-6363, Harari@humonc.wisc.edu

RTOG 0324 has been updated as follows:

Section 5.1.1 — The phrase “study-specific FDA 1572 form to” was inadvertently omitted from U.S. Pre-Registration Requirements. The paragraph should read “U.S. sites must mail or send overnight the completed, signed, original, study-specific FDA 1572 form to Coalition of National Cancer Cooperative Groups, 1818 Market Street, Suite 1100, Philadelphia, PA 19103.”

NOTE: This is an editorial/administrative change 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: http://www.rtog.org/
RTOG 0324, “Phase II Study Of Cetuximab (C225) In Combination With Chemoradiation In Patients With Stage IIIA/B Non-Small Cell Lung Cancer (NSCLC)”

Study Chair: George Blumenschein, M.D., (713) 792-6363, Harari@humonc.wisc.edu

RTOG 0324 has been updated as follows:

Section 5.1 — Updated to clearly define the procedures for submitting regulatory documents prior to patient registration.

Sections 5.1.3, 7.2.7 and Appendix IV — Updated to define how institutions must submit “Study Agent Shipment Form” prior to patient registration.

NOTE: This is an editorial/administrative change 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: http://www.rtog.org/
**SUMMARY OF CHANGES**

*Update, March 19, 2004*

**RTOG 0324**, “Phase II Study Of Cetuximab (C225) In Combination With Chemoradiation In Patients With Stage IIIA/B Non-Small Cell Lung Cancer (NSCLC)”

**Study Chair**: George Blumenschein, M.D., (713) 792-6363, Harari@humonc.wisc.edu

RTOG 0324 has been updated as follows:

**Section 5.1.1** - Updated to clearly define the procedures for submitting regulatory documents prior to patient registration.

**Sections 5.1.2, 7.2.7 and Appendix IV** – Updated to define where institutions must submit “Study Agent Shipment Form” prior to patient registration.

NOTE: This is an editorial/administrative change 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 (no password required) on the RTOG website: [http://www.rtog.org/](http://www.rtog.org/)