RTOG 0212, "A Phase II/III Randomized Trial Of Two Doses (Phase III-Standard Vs. High) And Two High Dose Schedules (Phase II-Once Vs. Twice Daily) For Delivering Prophylactic Cranial Irradiation For Patients With Limited Disease Small Cell Lung Cancer"

Study Chair: Aaron H. Wolfson, M.D., 305-243- 4210; FAX # 305-243-4363; awolfson@med.miami.edu

As mandated by CTEP, RTOG 0212 has been amended to replace CTC version 2.0 with the CTEP Active Version of CTCAE. Changes were made to the following sections:

- Section 6.5.1
- Appendix IV
- Appendix VI, Sections "B", "D" "E", and "Adverse Event Reporting for ECOG Investigators"
SUMMARY OF CHANGES
Update Date: June 12, 2008
(Broadcast 6/12/08)

**RTOG 0212**, "A Phase II/III Randomized Trial Of Two Doses (Phase III-Standard Vs. High) and Two High Dose Schedules (Phase II-Once Vs. Twice Daily) For Delivering Prophylactic Cranial Irradiation For Patients With Limited Disease Small Cell Lung Cancer"

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**RTOG 0212** has been updated as follows:

**Title page**: At SWOG's request, the SWOG Co-Chair was updated from Dr. Goldberg to Dr. Gaspar. In addition, the local number for RTOG Headquarters was replaced with the 800-number, per current RTOG standard.

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".
SUMMARY OF CHANGES
Amendment 6, Version Date: December 6, 2005

RTOG 0212, "A Phase II/III Randomized Trial Of Two Doses (Phase III-Standard Vs. High) And Two High Dose Schedules (Phase II-Once Vs. Twice Daily) For Delivering Prophylactic Cranial Irradiation For Patients With Limited Disease Small Cell Lung Cancer"

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The Institut Gustave-Roussy (IGR) is closing its phase III part of the study to patient accrual on December 31, 2005. The phase II part of the study will remain open to accrual. The protocol has been amended to address data management and statistical issues after the phase III closure. These changes are as follows:

Section 1.1: A paragraph was added at the end of the section stating that data for patients enrolled after December 31, 2005 will be managed by RTOG.

Section 1.4: A new section was added regarding data collection for patients enrolled after December 31, 2005, as well as for those enrolled on or before December 31, 2005.

Section 2.0: Objectives for patients enrolled on or before December 31, 2005, have been shaded in gray. Primary objectives for patients enrolled after December 31, 2005 were added.

Section 6.5: The statement "(for toxicities in patients who enrolled on or before 12/31/05)" was added for information to be faxed to the IGR.

Sections 13.1.1 and 13.1.2 were shaded in gray; they now apply only to patients enrolled on or before December 31, 2005.

Section 13.1.3: Primary endpoints were added for patients enrolled after 12/31/05.

Section 13.2.1 was shaded in gray; it now applies only to patients enrolled on or before December 31, 2005.

Section 13.2.2: Overview was added for patients enrolled after 12/31/05.

Section 13.4: The sentence regarding the rate of patient accrual and time to target accrual was revised based on December 1, 2005 data. A statement was added explaining that the phase III study met its target accrual and that the following (gray-shaded) paragraph is part of the original protocol and applies to patients enrolled from study activation through December 31, 2005.
Appendix I-Informed Consent: The original text under "Why Is This Study Being Done?" was highlighted in gray; this information now applies only to patients enrolled on or before December 31, 2005. A new paragraph was added for patients enrolled after December 31, 2005.

Appendix IX-Publication Policy: A paragraph was added regarding the timing of publication of the results of the two parts of the study (phase III and phase II). In the second paragraph, Statistical unit was changed to Department of Statistics.

Other Changes

Section 12.1: "Treatment planning Brain CT/MRI Report" was changed to "Pre-treatment Brain CT/MRI Report."

An amended protocol is available (no password required) on the RTOG Web site, http://www.rtog.org
The Institut Gustave-Roussy, based on the recommendation of its Steering Committee, has revised the ineligibility criteria of PCI 01-EULINT1, the international cranial irradiation companion study to RTOG 0212. The Steering Committee’s recommendation followed a serious adverse event (death) of a patient who had been receiving permanent oral medication for epilepsy and concerns regarding the use of thalidomide as an experimental drug in small cell lung cancer.

The ineligibility criteria of RTOG 0212 have been amended to correspond to the revision of PCI 01-EULINT1:

- Patients with epilepsy requiring permanent oral medication are excluded;
- Planned concurrent chemotherapy or antitumoral agent during PCI is not permitted.

The following sections were amended: “Eligibility” on the Schema page, page 1 of the Eligibility Checklist (Questions 12 and 16), and Sections 3.2.3 and 3.2.6.

Other Changes

Title page: The contact information for Dr. Movsas was updated.

An amended protocol is available (no password required) on the RTOG Web site, http://www.rtog.org
SUMMARY OF CHANGES
Revision 4, Version Date: July 8, 2004

RTOG 0212, “A Phase II/III Randomized Trial Of Two Doses (Phase III-Standard Vs. High) And Two High Dose Schedules (Phase II-Once Vs. Twice Daily) For Delivering Prophylactic Cranial Irradiation For Patients With Limited Disease Small Cell Lung Cancer”

Study Chair: Aaron H. Wolfson, M.D., 305-243- 4210; FAX # 305-243-4363; awolfson@med.miami.edu

The Cancer and Leukemia Group B (CALGB) is participating in this study.

The following changes were made for CALGB investigators:

- The CALGB study number and Co-Chair were added to the title page;
- Sections 5.5 and 12.5 were added;
- Sections 3.3, 6.1.7, 11.3.3, 11.4.1, and Appendix VIII were revised;
- In Appendix I, under “What About Confidentiality?”, CALGB was added to the organizations that may inspect and/or copy patient records.

Other changes:
Title page: The 800 number was deleted as this number will change when RTOG Headquarters moves in the near future.

Section 1.3.1: In the first sentence of the second paragraph, the phrase, “from SCLC who did and did receive”, was corrected to “from SCLC who did and did not receive”.

Section 12.0: The RTOG Headquarters address was updated.

A revised protocol is available (no password required) on the RTOG Web site, http://www.rtog.org
RTOG 0212, “A Phase II/III Randomized Trial Of Two Doses (Phase III-Standard Vs. High) and Two High Dose Schedules (Phase II-Once Vs. Twice Daily) For Delivering Prophylactic Cranial Irradiation For Patients With Limited Disease Small Cell Lung Cancer”

Study Chair: Aaron H. Wolfson, M.D., (305) 243- 4210, awolfson@med.miami.edu

RTOG 0212 has been updated as follows:

Section 11.4.1 – SWOG Institution contact updated to Lisa Headlee.

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”.

An updated protocol is available (no password required) on the RTOG website: http://www.rtog.org/
SUMMARY OF CHANGES
Revision 3, Version Date: December 9, 2003

RTOG 0212, “A Phase II/III Randomized Trial Of Two Doses (Phase III-Standard Vs. High) And Two High Dose Schedules (Phase II-Once Vs. Twice Daily) For Delivering Prophylactic Cranial Irradiation For Patients With Limited DiseaseSmall Cell Lung Cancer”

Study Chair: Aaron H. Wolfson, M.D., 305-243- 4210; FAX # 305-243-4363; awolfson@med.miami.edu

IRB Review Requirements:
(   ) Full board review required
(X) Expedited review allowed; however, site IRB requirements take precedence.
(   ) No review required

The Southwest Oncology Group (SWOG) and Eastern Cooperative Oncology Group (ECOG) are participating in this study.

The following changes were made for SWOG investigators:

• The SWOG Co-Chair was added to the title page;
• Sections 3.3, 5.3, 6.1.7, 11.3.3, and 12.3 were added;
• Sections 6.5, 11.4.1, and Appendix VIII were revised;
• In Appendix I, under “What About Confidentiality?”, SWOG was added to the organizations that may inspect and/or copy patient records.

The following changes were made for ECOG investigators:

• The ECOG Co-Chair was added to the title page;
• Sections 3.3, 5.4, 6.1.7, 11.3.3, 11.6.3, and 12.4 were added;
• Sections 11.4.1, 12.0, Appendix VI, and Appendix VIII were revised;
• In Appendix I, under “What About Confidentiality?”, ECOG was added to the organizations that may inspect and/or copy patient records.

Other changes:
Eligibility Checklist — Question 5, page 2 was updated to RTOG standard.

Section 12.0 — Data submission instructions were updated to RTOG standard.

Appendix I — Under “What About Confidentiality?”, RTOG was added to the organizations that may inspect and/or copy patient records.

A revised protocol is available (no password required) on the RTOG Web site, http://www.rtog.org
SUMMARY OF CHANGES
Revision 2, Version Date: August 6, 2003

RTOG 0212, “A Phase II/III Randomized Trial Of Two Doses (Phase III-Standard Vs. High) And Two High Dose Schedules (Phase II-Once Vs. Twice Daily) For Delivering Prophylactic Cranial Irradiation For Patients With Limited Disease Small Cell Lung Cancer”

Study Chair: Aaron H. Wolfson, M.D., 305-243- 4210; FAX # 305-243-4363; awolfson@med.miami.edu

IRB Review Requirements:
( ) Full board review required
(X) Expedited review allowed; however, site IRB requirements take precedence.
( ) No review required

RTOG 0212 has been revised as follows:

Eligibility Checklist — Question 6 on page 1 was deleted, as patients “may have started” but are not required to have begun consolidative chest irradiation by study entry (subsequent questions were appropriately renumbered); in addition, Section 3.1.5 was revised from “Patients may have at least started consolidative chest irradiation…” to “Patients may have started consolidative chest irradiation….”

Appendix I, under “What Is Involved In The Study”, the first paragraph was revised to correctly correspond to Section 13.2; the number of treatment days under “Treatment 1”, “Treatment 2”, and “Treatment 3” was revised to correctly correspond to the Schema and Section 6.0.

A revised protocol is available (no password required) on the RTOG Web site, http://www.rtog.org
SUMMARY OF CHANGES
Revision 1, Version Date: April 3, 2003

RTOG 0212, “A Phase II/III Randomized Trial Of Two Doses (Phase III-Standard Vs. High) And Two High Dose Schedules (Phase II-Once Vs. Twice Daily) For Delivering Prophylactic Cranial Irradiation For Patients With Limited Disease Small Cell Lung Cancer”

Study Chair: Aaron H. Wolfson, M.D., 305-243-4210; FAX # 305-243-4363; awolfson@med.miami.edu

IRB Review Requirements:
( ) Full board review required
(X) Expedited review allowed; however, site IRB requirements take precedence.
( ) No review required

RTOG 0212 has been revised as follows:

Title page — The title was revised for clarity; this change also was made to the title on the Schema page, on the first page of Appendix I (the sample consent form), and in Appendix VIII.

Schema page
- In the stratification variable, “Interval from induction therapy to randomization”, number 3 was revised from “> 180 days” to “181-240 days” to more clearly define patient eligibility; corresponding changes also was made in question 17, page 2 of the Eligibility Checklist, in Section 3.1.3, and in the last sentence of Section 13.2.
- In the Eligibility list on the Schema page, the third bullet was corrected to more closely correspond with the International Cranial Irradiation Trial protocol.

Section 2.0 — Parenthetical phrases were added to Sections 2.1 and 2.2 to clearly indicate which phase of the study correlates with the study objectives; this change also was made in Section 13.1.

A revised protocol is available (no password required) on the RTOG website: http://www.rtog.org/
RTOG 0212, “A Phase II/III Randomized Trial Of Two Dose Schedules For Delivering Prophylactic Cranial Irradiation For Patients With Limited Disease Small Cell Lung Cancer”

Study Chair: Aaron H. Wolfson, M.D., (305) 243-4210, awolfson@med.miami.edu

RTOG 0212 has been updated as follows:

Eligibility Checklist, page 2 – Questions 5 and 10 were updated to RTOG standard; question 16 was deleted from this operational/demographic portion of the checklist.

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”.

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