SUMMARY OF CHANGES
Update Date: September 15, 2011
(Broadcast Date: September 15, 2011)

RTOG 0537, “A Phase II/III Study Comparing Acupuncture-like Transcutaneous Electrical Nerve Stimulation (ALTENS) Versus Pilocarpine in Treating Early Radiation-Induced Xerostomia”

Study Chair: Raimond K. W. Wong, MD; 905-387-9495, x64704; raimond.wong@jcc.hhsc.ca; wongrai@mcmaster.ca

RTOG 0537 has been updated as follows:

Due to issues with the e-mail system at his institution, an alternate e-mail address (wongrai@mcmaster.ca) has been added to the protocol title page for Dr. Wong. Sites may use this e-mail address to contact Dr. Wong regarding the protocol.
RTOG 0537, “A Phase II/III Study Comparing Acupuncture-like Transcutaneous Electrical Nerve Stimulation (ALTENS) Versus Pilocarpine in Treating Early Radiation-Induced Xerostomia”

Study Chair: Raimond K. W. Wong, MD; 905-387-9495, x64704; raimond.wong@jcc.hhsc.ca

RTOG 0537 has been amended as follows:

As mandated by NCI, Section 7.4 (first paragraph) has been amended to require the use of CTCAE version 4 for grading of all adverse events reported via AdEERS as of October 1, 2011. All AE reporting on the study case report forms (CRFs) should follow grading criteria instructions on the specific CRF.

Other Changes

Global: All web links and related descriptions to sub-pages of the RTOG web site were updated.

Title Page: Dr. Shook is now the senior statistician for this trial; Dr. Shook’s contact information was added to the title page. Also, the protocol document history table was added per RTOG standard.

Section 5.2.1: Details regarding regulatory document translation added per current RTOG regulatory processes.

Section 5.3.1: The RTOG web support e-mail address in the next to last paragraph was updated.

Section 7.4.3: Revised as required per current NCI reporting requirements for acute myeloid leukemia (AML) or myelodysplastic syndrome (MDS) via AdEERS.

Appendix I (Sample Consent):

- **Will my medical information be kept private?**
  Per NCI, the paragraph beginning “A description of this clinical trial will be available…” [new FDA language per 21 CFR 50.25(c)] and the “Note to Informed Consent Authors” were inserted to provide additional details to participants and the local institution.

- **Where can I get more information?**
  The NCI’s TTY number is no longer in service and was deleted.
SUMMARY OF CHANGES
Update: August 3, 2010
(Broadcast August 3, 2010)

RTOG 0537, A Phase II/III Study Comparing Acupuncture-like Transcutaneous Electrical Nerve Stimulation (ALTENS) Versus Pilocarpine in Treating Early Radiation-Induced Xerostomia

Study Chair: Raimond K. W. Wong, MD, 905-387-9495, x64704, raimond.wong@jcc.hhsc.ca

RTOG 0537 has been updated as follows:

Title Page: The following was added to the top of the page, "Note: Due to the limited number of Codetron® units this is a limited-institution study with pre-selected sites".

Schema: To be consistent with Section 3.1.3, the third stratification option for "time from cancer treatment" was revised from > 1 year to 1-2 years.

Section 5.1.1: In the first sentence of the first paragraph, "register 2 eligible patients" was revised to "register 1 eligible patient". In the first sentence of the second paragraph, "at least 2 patients" was revised to "at least 1 patient". This change was made to allow the first patient to begin their treatment immediately.

Section 7.2.7: Consistent with the changes made to Section 5.1.1, in the first sentence of the second paragraph, "register 2 eligible patients" was revised to "register 1 eligible patient". In the first sentence of the third paragraph, "at least 2 patients" was revised to "at least 1 patient".

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 an amendment.
SUMMARY OF CHANGES
Amendment 1: August 26, 2009
(Broadcast September 17, 2009)

RTOG 0537, A Phase II/III Study Comparing Acupuncture-like Transcutaneous Electrical Nerve Stimulation (ALTENS) Versus Pilocarpine in Treating Early Radiation-Induced Xerostomia

Study Chair: Raimond K. W. Wong, MD, 905-387-9495, x64704, raimond.wong@jcc.hhsc.ca

RTOG 0537 has been amended as follows:

Section 3.1

- 3.1.2: Was revised in response to feedback from investigators that after one year of follow-up, routine imaging tests are not commonly indicated for patients who have no evidence of head and neck cancer recurrence based on a complete physical, including head and neck examination.
- 3.1.3: Was revised to clarify that patients could have received cancer treatment (radiotherapy with or without chemotherapy) up to a maximum of 2 years but no less than 3 months prior to study entry. Also, "salivary gland changes/saliva xerostomia scale" was deleted to remove the confusion regarding measured salivary flow and symptoms using the CTCAE v.3. As a result of this change, the salivary flow measurement criteria has been revised to "equal or greater than 0.1 ml/min" in Section 3.1.4.
- 3.1.5: The drug "cevimeline" was added to the eligibility section. Patients who have received cevimeline are eligible for participation (in the Phase III component of the study), but must discontinue use within 2 weeks prior to randomization.

As a result of the changes to Section 3.1, changes were also made to the text under "Patient Population" on the Schema page and to questions 2, 3, 4, 5, and 9 on page 1 of the Eligibility Checklist.

Other changes made to the protocol include:

Title Page: Dr. Sagar's telephone extension number was updated. Dr. Zhang has replaced Dr. Pajak as the Senior Statistician for this protocol.

Eligibility Checklist: Question 14 on page 2 was revised to the new standard language for this item.

Section 3.0
• **3.2.1 and 3.2.9**: Specify that patients with chronic lymphocytic leukemia and Sjögrens Syndrome, respectively, are not eligible. Questions 9 and 21 on pages 1 and 2 of the *Eligibility Checklist* were revised as a result.

• **3.2.6**: "Regular" was added before "medications", for clarity.

**Section 5.0**

• **5.1.1 and 7.2.7**: In the first sentence of the first paragraph, "identify" was revised to "register" for clarity to institutions that at least two eligible patients must be enrolled on study before a Codetron® unit will be shipped to the institution. Also, the RTOG Headquarters contact telephone number in the last sentence was revised. In addition, *Appendix VI* was removed as the last page of the protocol. It will be posted separately on the RTOG web site next to the protocol. These sections were updated to include this information.

• **5.2**: The section numbering for Section 5.2.1 was corrected (from 5.1.1 to 5.2.1). Other changes were made to this section as a result of revision of the standard RTOG Protocol Template since the protocol was activated.

• **5.3.1**: The RTOG "web support" e-mail address was updated.

**Section 7.0**

• **7.1**: For clarity, the sentence beginning "The Phase II component of the trial…” was added immediately before the section.

• **7.2.4**: Additional text was added to this section to provide more information about the ALTENS therapy treatment schedule.

• **7.2.7**: The first sentence of the first paragraph was revised to indicate that participating sites will receive 2 sets of electrodes with the shipment of the Codetron® unit.

**Section 11.0**

• **11.1**: The last two sentences in the paragraph immediately preceding this section were added as a result of revision of the standard RTOG Protocol Template since the protocol was activated.

• **11.4.3.1**: In the first sentence, "one and a half hour" was revised to "two hours", for consistency with Section 3.1.4.

**Section 12.1**: In the Data Submission table, "Phase III only" was added next to "UWHNSS (HP)" in the top and bottom boxes of the table. "Phase III only" was also added to the Study Parameter Table in *Appendix II*.

**Section 13.0**

• **13.2.2.2**: In the second paragraph, "69 months" was corrected to "9 months". Also, in the next to the last sentence of the third paragraph, "0.50" was corrected to "0.05".
• **13.3**: In the first paragraph, "43 patients" was corrected to "45 patients".

**Appendixes**

• **I (Sample Consent):**
  
  - Under "Before you begin the study", information regarding the salivary production assessment (taken from "Part B treatment/Prior to first treatment"), was added to the fourth bulleted item, for clarity to the participant.
  - Under "How long will I be in the study/Patients taking part in Part A", "ALTENS" was added in parentheses next to "treatment" for clarity to the participant.

• **II (Study Parameter Table):**
  
  - "Phase III only" was added to the "Follow up" column in place of the "X" for "Whole Salivary Production" and to the "Pre-treatment and Follow up" columns in place of the "X" for the "The Head and Neck Symptom Scale of the University of Washington Quality of Life Questionnaire (UWHNSS)" assessment to clarify to institutions when these assessments must be conducted.
  - In the XeQOLS row/Follow-Up column, "At 6 months only during Phase II" was added for clarity to institutions.

• **III (Performance Scale):** REFERENCES to the Karnofsky scale were deleted per current RTOG standard (Zubrod scale).

• **VI (Accrual Agreement):** Was revised for clarity to sites regarding patient enrollment and shipping of the Codetron® machine. Also, the RTOG Headquarters contact number was corrected. In addition, this appendix was removed as the last page of the protocol. It will be posted separately on the RTOG web site next to the protocol. (See changes for Sections 5.1.1 and 7.2.7 above.)