RTOG 0831, “A Randomized, Double-Blinded, Placebo-Controlled Phase III Trial To Evaluate The Effectiveness Of A Phosphodiesterase 5 Inhibitor, Tadalafil, In Prevention Of Erectile Dysfunction In Patients Treated With Radiotherapy For Prostate Cancer [Prevention of Erectile Dysfunction Study (PEDS)]”

Study Chair: Deborah Watkins Bruner, PhD, RN, FAAN, 404-712-9695, deborah.w.bruner@emory.edu

RTOG 0831 has been amended as follows:

Title Page: The contact information for the Principal Investigator, Dr. Bruner, was updated. Dr. Pugh has replaced Dr. Hunt as the Senior Statistician for the study; her contact information was added. Protocol document history table added, per RTOG format.

Eligibility Checklist: Page 1 question 3, “The not applicable (NA)” option was added.

Section 3.1.9: The eligibility criterion regarding completion of the IIEF (QF form) was deleted; the corresponding Eligibility Checklist question # 10 also was deleted. The subsequent questions were renumbered in Section 3.1 and in the Eligibility Checklist.

Section 7.2.5: Biologics, Inc. information updated.

Section 7.5: Last paragraph before subsection 7.5.1 was inserted.

Section 7.5.1: Updated the reference to the “NCI Guidelines: Adverse Event Reporting Requirements” document.

Section 7.5.2: The first paragraph and bulleted text and the last sentence of the last paragraph were deleted.

Section 7.5.3: Updated.

Section 10.2.4: Updated the street address for the RTOG Biospecimen Resource.

Section 12.1: Dose Volume Histogram and time frame for submission added to the Data Submission table.

Section 13.4.2.2: Details regarding missing data for the IIEF were added to the analysis plan.

Appendix V: Updated the street address for the RTOG Biospecimen Resource.

Appendix VI: The CTSU RT Facilities Inventory Form was added to the bulleted list of “Requirements for RTOG 0831 site registration”. The “Note” regarding the RPC and the RT Facilities Inventory Form was inserted below it.
SUMMARY OF CHANGES
Amendment 2, Version Date: April 25, 2011
(Broadcast: May 10, 2011)

RTOG 0831, “A Randomized, Double-Blinded, Placebo-Controlled Phase III Trial To Evaluate The Effectiveness Of A Phosphodiesterase 5 Inhibitor, Tadalafil, In Prevention Of Erectile Dysfunction In Patients Treated With Radiotherapy For Prostate Cancer [Prevention of Erectile Dysfunction Study (PEDS)]”

Study Chair: Deborah Watkins Bruner, PhD, RN, FAAN, 215-746-2356, wbruner@nursing.upenn.edu

RTOG 0831 has been updated as follows:

RTOG 0831 is supported by the CTSU. CSTU participation language has been added to the following sections of the protocol: Cover page, Index page, Appendices I and IA (under “Will my medical information be kept private”), Appendix VI

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

Cover page: Dr. Hunt’s e-mail address was updated.

Section 5.4.1.1: This subsection regarding translation of regulatory documents was added, per RTOG standard.

Section 5.5.1: The RTOG web support address in the next to last paragraph was updated.
SUMMARY OF CHANGES

Update: September 7, 2010

(Broadcast: September 7, 2010)

RTOG 0831, "A Randomized, Double-Blinded, Placebo-Controlled Phase III Trial To Evaluate The Effectiveness Of A Phosphodiesterase 5 Inhibitor, Tadalafil, In Prevention Of Erectile Dysfunction In Patients Treated With Radiotherapy For Prostate Cancer [Prevention of Erectile Dysfunction Study (PEDS)]"

Study Chair: Deborah Watkins Bruner, PhD, RN, FAAN, 215-746-2356, wbruner@nursing.upenn.edu

RTOG 0831 has been updated as follows:

Eligibility Checklist: Page 1, question 12, the "N" was inadvertently omitted as a response option; it was inserted for consistency with the eligibility criteria in Section 3.1.11.
**SUMMARY OF CHANGES**  
**Amendment 1: August 20, 2010  
(Broadcast: September 7, 2010)**

**RTOG 0831**, "A Randomized, Double-Blinded, Placebo-Controlled Phase III Trial To Evaluate The Effectiveness Of A Phosphodiesterase 5 Inhibitor, Tadalafil, In Prevention Of Erectile Dysfunction In Patients Treated With Radiotherapy For Prostate Cancer [Prevention of Erectile Dysfunction Study (PEDS)]"

**Study Chair**: Deborah Watkins Bruner, PhD, RN, FAAN, 215-746-2356, wbruner@nursing.upenn.edu

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**RTOG 0831** has been amended as follows:

**Schema**: An asterisk was added next to "radiation therapy" under "Arm 2".

**Eligibility Checklist**:

- Page 1, question 2, "NA" was added as a response option, for consistency with the eligibility criteria in Section 3.1.2.
- Page 1, question 9, was revised for consistency with changes made in Sections 3.1.7 and 6.1.1.
- Page 3, top of page, a note regarding pre-registration IMRT and/or brachytherapy credentialing requirements was added. **IMRT and/or brachytherapy credentialing will be required **only** if IMRT and/or brachytherapy will be used to treat the patient.**
- Page 4, question 24, was revised so institutions can specify if IMRT or protons will be used. Also, the parenthetical notations regarding credentialing requirements were added for clarity.

**Section 1.7**: In the second paragraph beneath Table 1, the tadalafil dosage specified in the sentence beginning, "In the proposed study;K" was corrected to 5 mg.

**Section 3.1.8**: The allowed external beam RT treatment dose specified in the section was revised from "between 72 Gy and 79.2 Gy" to "between 75 Gy and 79.2 Gy", to be consistent with National Comprehensive Cancer Network Clinical Practice Guidelines.

**Sections 5.1 to 5.3**: Added pre-registration credentialing requirements text for IMRT, 3D-CRT, and brachytherapy treatment approaches. The subsequent sections were renumbered.

**Section 6.0**:

- At the beginning of Section 6.0, the statement, "Protocol treatment must begin within 30 days after randomization" was revised to "Protocol treatment must
begin within 6 weeks after randomization". Also, a "note" about RT pre-registration credentialing requirements was added.

- **Sections 6.1 and 6.2:** These sections were expanded to maintain consistency in context and formatting with another prostate cancer population study, RTOG 0815.

**Section 7.5:** As mandated by the NCI Division of Cancer Prevention (DCP), "CTEP Active Version" was replaced with the current CTCAE version number, "CTCAE version 4".

**Section 10.3:** The RTOG reimbursement text was updated. The updated text includes a web address for the Reimbursement and Case Credit Schedule located on the RTOG website.

The following subsections of **Section 10.0** were revised according to current RTOG Biospecimen Resource specimen collection procedures.

- **Sections 10.1, 10.2.1, and 10.2.3:** Whole blood specimens will be collected instead of buffy coat. "Whole blood" replaces "buffy coat" in each of these sections.
- **Section 10.2.2:** The specimen shipping days for Canadian sites (Monday-Tuesday only) were added.
- **Section 10.2.4:** The shipping address for non-frozen specimens was deleted because only frozen specimens are being collected in this trial.

**Section 12.1:** The "note" regarding site archival of digital RT data and RTOG Headquarters' request for digital RT data submission was added at the bottom of the section.

**Sections 13.1.2.6 and 13.4.2.6:** As mandated by the NCI Division of Cancer Prevention (DCP), "CTEP Active Version" was replaced with the current CTCAE version number, "CTCAE version 4".

**Section 13.2.2:** In the last sentence of the second paragraph, the attrition rate was corrected from 20% to 15%.

**Appendix I (Sample Consent):**

- Under "What side effects or risks can I expect from being in the study/risks and side effects related to tadalafil", the risk of, "painful erection that won't go away (priapism)" was moved from the list of "rare" side effects to the list of "rare but serious" side effects. This change is consistent with the Lilly prescribing information for tadalafil.
- For clarity, under "What side effects or risks can I expect from being in the study/Rare but serious": "in rare cases, may become permanent" was added in parentheses next to "decreased hearing, hearing loss".
• Under "Quality of Life Study", third paragraph: the International Index of Erectile Function Questionnaire (IIEF) was removed. The IIEF questionnaire is a part of the main study only; it is not a component of the Quality of Life study. In the next paragraph beginning, "Married patients and their spouses;K", the phrase, "a third questionnaire" was replaced with "another questionnaire" as a result of the removal of the IIEF from the paragraph above it.

Appendix IA (Sample Consent, QOL-Spouses/Partners):

• Under "What will happen if I take part in this research study;K?", first paragraph: the International Index of Erectile Function Questionnaire (IIEF) was removed. The IIEF questionnaire is a part of the main study only; it is not a component of the Quality of Life study.
• In the first sentence of the next paragraph beginning, "Spouses or partners living as married;K", the phrase, "a third questionnaire" was replaced with "another questionnaire" and "above questionnaires" was replaced with "SAQ-P" as a result of the removal of the IIEF from the paragraph above it.
• In the first sentence of the next paragraph beginning, "Spouses or partners living as married;K", "or partner" was inserted after "spouse" in the list of questionnaire assessment times.

Appendix V (Blood Collection Kit Instructions): Updated according to current RTOG Biospecimen Resource specimen collection procedures.