For **Protocol** Amendment #3 to: **RTOG 0621**, Adjuvant 3DCRT/IMRT in Combination With Androgen Suppression and Docetaxel for High Risk Prostate Cancer Patients Post-Prostatectomy: A Phase II Trial

NCI/Local Protocol #: RTOG-0621/RTOG 0621

NCI Protocol Version Date: April 16, 2014  (Broadcast Date: April 28, 2014)

<table>
<thead>
<tr>
<th>Section</th>
<th>Change</th>
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<tbody>
<tr>
<td>Title page</td>
<td>Due to the transition to the NCI National Clinical Trials Network (NCTN), references to “RTOG” were replaced with “NRG Oncology”.</td>
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<td>Schema page</td>
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<td>Section 12.0</td>
<td>The Principal Investigator, Dr. Hurwitz, has moved to a new institution. His contact information was revised. Dr. Zhang has replaced Dr. Hunt as the study senior statistician.</td>
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<td>7.9</td>
<td>As required by CTEP, references to the “Adverse Event Reporting System (AdEERS)” have been changed to “CTEP Adverse Event Reporting System (CTEP-AERS)” throughout these sections. RTOG terminology was revised to NRG Oncology terminology where applicable.</td>
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<td>7.10</td>
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SUMMARY OF CHANGES
Amendment 2, Version Date: December 23, 2010
(Broadcast: January 11, 2011)

RTOG 0621, Adjuvant 3DCRT/IMRT in Combination with Androgen Suppression and Docetaxel for High Risk Prostate Cancer Patients Post-Prostatectomy: A Phase II Trial

Study Chair: Mark Hurwitz, M.D., (508) 235-5700, mhurwitz@lroc.harvard.edu

RTOG 0621 has been amended as follows:

As mandated by CTEP, CTCAE version 3.0 reporting requirements in Section 7.9 of the protocol will be converted to CTCAE version 4 for grading of all adverse events reported via AdEERS beginning January 1, 2011. All case report forms will continue to use CTCAE version 3.0.

Note: REFERENCES to CTCAE, version 3.0, may remain in the protocol. These are appropriate, as treatment decision for patients enrolled on this study were based on that version.

Other Changes
Title Page: Dr. Hunt's e-mail address was updated.

Section 7.9.3: This section was amended as required by CTEP to instruct sites to report AML or MDS via AdEERS.
RTOG 0621, Adjuvant 3DCRT/IMRT in Combination with Androgen Suppression and Docetaxel for High Risk Prostate Cancer Patients Post-Prostatectomy: A Phase II Trial

Study Chair: Mark Hurwitz, M.D., (508) 235-5700, m hurwitz@lroc.harvard.edu

RTOG 0621 has been updated as follows:

Sections 7.2.5.1, 7.3.6.1, 7.4.6.1, 7.6.6.1: Supply information for commercially available drugs was updated for non-Canadian international institutions per current RTOG standard.
RTOG 0621, Adjuvant 3DCRT/IMRT in Combination with Androgen Suppression and Docetaxel for High Risk Prostate Cancer Patients Post-Prostatectomy: A Phase II Trial

**Study Chair:** Mark Hurwitz, M.D., (508) 235-5700, mhurwitz@lroc.harvard.edu

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**RTOG 0621** has been amended as follows:

**Title Page:** Dr. Shayegan was added as the urology co-chair, the senior statistician was changed from Dr. Bae to Dr. Hunt.

**Eligibility Checklist, Page 3 of 3, Question 19:** "Pre-consent" was corrected to "pre-registration."

**Section 3.2.3:** The spelling of dutasteride was corrected.

**Sections 3.1.5.2 and 11.3.4:** For clarity, a statement was added indicating that the use of contrast is at the discretion of treating physician.

**Section 4.0:** The text for the specimen collection removed, and a statement was added indicating that pre-treatment evaluations/management separate from eligibility is not applicable to this study. Per current RTOG standard, information regarding specimen collection and timeline is located in Section 10.

**Sections 5.1.1-5.3.4.2:** IMRT, 3DCRT, and regulatory pre-registration requirements were updated to current RTOG standard.

**Section 6.5:** The spelling of interpolation and interpolations was corrected.

**Section 6.9:** Heading: "Therapy" was added after "Radiation" for clarity.

**Sections 7.2.5.1, 7.3.6.1, 7.4.6.1, 7.5.6.1.1, 7.5.7.2.1, 7.6.6.1:** Supply information was added for Non-Canadian international institutions per current RTOG standard.

**Section 7.5.7.1:** Contact information was updated for Sanofi-Aventis.

**Section 7.5.7.2:** 3rd paragraph: The note for international sites was deleted due to the information added in Section 7.5.7.2.1 as described above.

**Section 7.9.1:** 1st paragraph: The NCI Guidelines reference was updated to January 2005.
Section 7.9.2: Definition of SAE, last sentence: Pregnancy was added per current RTOG standard.

Section 7.10: The 1st paragraph was added per current RTOG standard.

Section 10.0: The 2nd paragraph/note was added per current RTOG standard.

Section 10.2.1.1: The 1st paragraph and 1st bullet were updated per current RTOG standard.

Section 10.2.1.2: 20 °C was corrected to -80 °C.

Section 10.2.1.3: The 1st row was updated per current RTOG standard.

Sections 10.3 and Appendix V: Contact information was updated for RTOG Biospecimen Resource.

Section 10.4: The 1st sentence updated per current RTOG standard.

Section 11.2.4: 1st sentence: "Chemistry" was expanded to "CBC/differential and ANC, AST, ALT, alkaline phosphatase, and bilirubin" for clarity.

Section 11.3.1: 1st sentence: "Until the end of year 3" was corrected to "until the end of year 2."

Section 11.3.2: 1st sentence: "A PSA should be obtained after year 2, every 6 months…" was corrected to "After year 2, a PSA should be obtained every 6 months…"

Section 12.1: The Treatment Summary Form (TF) was added.

Section 12.2: The logistics for Dosimetry Digital Data Submission was updated to current RTOG standard.

Section 13.1.1: In the last sentence, "with" was changed to "without."

Section 13.2: In the 1st sentence, "thereby i warranting" was corrected to "thereby warranting."

Section 13.4.1: The numbers in Table 1 were changed to correspond to 69, the number of eligible, analyzable patients. Original numbers were based on the adjusted number, 76, which included ineligible, unanalyzable patients.

Appendix I/Sample Consent

- During hormone therapy, radiation therapy, and chemotherapy treatment, 3rd paragraph: Sentences 6-7 were corrected to indicate that hormone treatment with
an LHRH agonist and flutamide or bicalutamide continues for 2 months following radiation completion.

- **During hormone therapy, radiation therapy, and chemotherapy treatment**, 4th paragraph, 1st sentence: "28 days after radiation ends" was corrected to "3-6 weeks after radiation ends."

- **When you are finished receiving treatment**, 1st sentence: "Every 6 months for years 2 through 5" was corrected to "every 6 months for years 3 through 5."

- **When you are finished receiving treatment**, last 2 sentences: The timing was corrected for blood draws for testosterone levels.

- **Study Plan**: "Flutamide or Bicalutamide; Leuprolide or Goserelin" was moved from the last box to the first box for clarity.

- **How long will I be in the study?** A new paragraph was added between "…almost 8 weeks" and "About 3-6 weeks" for clarity.

- **How long will I be in the study?** 3rd paragraph, 1st sentence: A comma was added after "every 3 months for 2 years" for clarity.

- **How long will I be in the study?** 3rd paragraph, 1st sentence: "Finishing treatment then yearly after 5 years" was changed to "finishing treatment, and then yearly after 5 years" for clarity.

- **Risks and side effects related to docetaxel**, rare but serious: "Changes in sensation in the nerves of the hands and feet" was deleted because it is included in the likely category.

- **Consent Form for Use of Tissue, Blood, and Urine for Research, Making Your Choice**: Questions 1 and 2 were expanded per current RTOG standard.

**Appendix III/Performance Scale**: References to the Karnofsky scale were deleted per current RTOG standard for studies using the Zubrod scale.

**Appendix V**: The content of the appendix was switched to Blood Collection per current RTOG Biospecimen Resource standards. The **Table of Contents** was appropriately renamed.

**Appendix VI**: The content of the appendix was switched to Urine Collection per current RTOG Biospecimen Resource standards. The **Table of Contents** was appropriately renamed.
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Study Chair: Mark Hurwitz, M.D., (508) 235-5700, mhurwitz@lroc.harvard.edu

RTOG 0621 has been updated as follows:

Instructions for the submission of the Canadian study agent shipment form were updated in Sections 5.3.3, 7.5.6, 7.5.7.2, and Appendix VII.

Other Changes

Title page: The name and contact information of the study statistician was added to update the protocol to current RTOG standard.

Section 7.5.7.1: The contact information for Sanofi-Aventis was updated.

Section 12.1: The interim Follow-up Form (FS) was deleted. Data will be submitted via the Initial Follow-Up Form (F0) for which the timeframe was updated.

Appendix II: The footnote, "*And as needed based on reporting requirements", was deleted as it is no longer RTOG standard and as adverse event evaluations are specified in the protocol text.

Note: These are editorial/administrative changes to the protocol. NCI now requires that these changes be documented on the protocol title page as "Update Date".