SUMMARY OF CHANGES  
Amendment 3: August 17, 2011  
(Broadcast: August 25, 2011)

RTOG 0529, "A Phase II Evaluation of Dose-Painted IMRT in Combination with 5-Fluorouracil and Mitomycin-C for Reduction of Acute Morbidity in Carcinoma of the Anal Canal"

Study Chair: Lisa Kachnic, MD; 617-638-7070; lisa.kachnic@bmc.org

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**RTOG 0529** has been amended as follows:

As mandated by CTEP, this study will utilize CTCAE version 4.0 for AdEERS reporting of adverse events beginning October 1, 2011. Related changes were made to **Section 7.6**.

**All AE reporting on the study 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.

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**Other Changes**

**Global**: All weblinks and related descriptions to sub-pages of the RTOG website were updated.

**Title Page**: The Document Version History table was added per current RTOG standard

**Section 7.6.3**: Text referring to AML/MDS paper report forms has been removed since AdEERS will now be used for reporting AML or MDS and additional notification to CTEP is no longer required. Instructions for submitting a hard copy of the report, including the RTOG HQ address, have also been deleted per current RTOG standard
RTOG 0529, "A Phase II Evaluation of Dose-Painted IMRT in Combination with 5-Fluorouracil and Mitomycin-C for Reduction of Acute Morbidity in Carcinoma of the Anal Canal"

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RTOG 0529 has been updated as follows:

Section 10.0 and Appendix VI: All references to and contact/shipping information for the RTOG Tissue Bank (at LDS Hospital) have been changed to the RTOG Biospecimen Resource at the University of California San Francisco.
SUMMARY OF CHANGES
Amendment #2: October 11, 2007

RTOG 0529, "A Phase II Evaluation of Dose-Painted IMRT in Combination with 5-Fluorouracil and Mitomycin-C for Reduction of Acute Morbidity in Carcinoma of the Anal Canal"

Study Chair: Lisa Kachnic, MD; 617-638-7070; lisa.kachnic@bmc.org

RTOG 0529 has been amended as follows:

Section 7.4 was modified: (1) to clarify existing dose modifications for grade 4 diarrhea, grade 3 and 4 mucositis/stomatitis, and grade 3 ANC/platelet toxicity; and (2) to add dose modifications for grade 4 ANC/platelet toxicity. Changes were made to the following places:

- **Diarrhea row/Grade 4/Modification column**: Reference to footnote b was added after "decrease dose 50%.”
- **Mucositis/Stomatitis row/Grade 3/Modification column**: Reference to footnote a was added after "decrease dose 50%."
- **Mucositis/Stomatitis row/Grade 4/Modification column**: Reference to footnote a was added after "decrease dose 50%.”
- **ANC or Platelets row/Grade 3/Modification column**: Reference to footnote e was added after "decrease dose 50%" and "decrease dose next cycle by 50%" was deleted.
- **ANC or Platelets row/Grade 4**: This text was added.
- **Footnote b**: The first two sentences were added.
- **Footnote e**: This text was added.

Appendix I, Risks and side effects related to the Chemotherapy (5-FU and Mitomycin)/Likely:

- **8th bullet**: Bruising or bleeding was deleted from the description of low white blood cell count because it was included in error.
- **10th bullet**: Low platelet count was added because it was inadvertently omitted.
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RTOG 0529 has been updated as follows:

Eligibility Checklist, 2nd section, question 20: Options for nodal status added
SUMMARY OF CHANGES
Amendment #1: May 31, 2007

RTOG 0529, "A Phase II Evaluation of Dose-Painted IMRT in Combination with 5-Fluorouracil and Mitomycin-C for Reduction of Acute Morbidity in Carcinoma of the Anal Canal"

Study Chair: Lisa Kachnic, MD; 617-638-7070; lisa.kachnic@bmc.org

RTOG 0529 has been amended as follows:

The treatment regimen was modified to clarify that chemotherapy begins on calendar day 29 and not day 29 of radiation therapy. Changes were made to the following sections:

Schema: "of RT" deleted from description of mitomycin-C and 5-FU; "(M-F)" added after "continuous infusion"; "note" text replaced with "Day 1 and 29 are based on calendar days"

Section 7.0: Second paragraph: "beginning day 29 of radiation therapy" changed to "on calendar day 29"

Section 7.3: "of RT" deleted from description of mitomycin-C and 5-FU

Appendix I, Sample Consent, What Will Happen If I Take Part in This Research Study?/Chemotherapy: Last sentence of first paragraph: "of RT" deleted

Optional (but strongly encouraged) serum, plasma, buffy coat, and urine collection has been added. Changes were made to the following sections:

Index: Appendix VI added

Eligibility Checklist, 2nd section, questions 18-19: Blood and urine added

Section 10.1-10.2.1.4: Reworded/renumbered

Section 10.2.2: Added

Section 10.2.3: Added

Section 10.2.4: Added

Section 10.2.5: Added

Section 10.2.6: Added

Section 10.2.7: Renumbered

Section 10.3: First sentence: Relevant reimbursement amounts added
Appendix I: Consent for Use of Tissue for Research: Reworded to reflect additional specimen collection and per RTOG standard

Appendix VI: Added

The following additional changes were made:
Eligibility Checklist, 1st section, question 4: Reworded due to modification in Section 3.1.2.2

Eligibility Checklist, 1st section, question 12: Reworded to be consistent with Section 3.1.9

Eligibility Checklist, 1st section, question 16: Reworded due to modification in Section 3.2.5

Eligibility Checklist, 2nd section, question 22: Added because nodal status needs to be collected for this protocol

Section 3.1.2.2: Colonoscopy added because any scope of the anal canal is acceptable, including colonoscopy

Section 3.2.5: "Prior surgery for cancer of the anus other than a diagnostic biopsy" changed to "Prior surgery for cancer of the anus that removed all macroscopic anal cancer" to reflect the possibility that prior surgery may have been performed for fistulas, condylomas, or smaller anal cancers but that macroscopic cancer still remains

Section 6.0: "Tomotherapy is allowed" added for increased clarity

Section 6.5.1: Second sentence of "note" added for increased clarity

Section 6.1.5: Planning priorities rewritten to clarify that the tumor planning goals must be met before the normal tissue (small bowel and femoral head) planning goals

Section 6.6.1: Imaging documentation requirements were clarified, with an additional section on tomotherapy imaging requirements included

Section 6.7.1.2: Cross reference corrected to 6.5.1.1

Section 6.7.1.3: Cross reference corrected to 6.5.1.2

Section 7.0: Second paragraph, third sentence added; since chemotherapy is set according to calendar day, this change was made to assure that a 3-week interval between chemotherapy cycles (cycle 1 and 2) will be maintained if an extended treatment break (5 or more days) ensues post administration of cycle 1 of chemotherapy due to neutropenia
and/or other causes

Section 7.2.2: Second paragraph, second-to-last sentence: "affected" corrected from "effected"

Section 7.4, Table

- "Modification" column: "Hold until resolved to \( \leq \) Grade 2" deleted from all rows (diarrhea, mucositis, stomatitis, ANC or platelets) for increased clarity and accuracy
- "Other Non-Hematologic" row: Deleted so that the protocol and resulting analysis are consistent with this trial's predecessor, RTOG 9811
- "Hematologic" row: Changed to "ANC or Platelets" for increased clarity and accuracy; "decrease next cycle by 50%" added in "modifications" section for increased clarity and accuracy
- Footnotes c and d added and referenced in "modification" column for increased clarity

Section 8.1.1: 1st bullet, second sub-bullet: 12-week time frame deleted for increased clarity and accuracy

Section 8.1.2: Last sentence: Clarified that APR is recommended in cases of pathologically confirmed residual disease

Section 13.2.5.1: Capitalization of heading corrected for consistency with the rest of the protocol

Appendix I, "What will happen if I take part in this research study?"/Before you begin this study: Last sentence of 5th bullet deleted because lymphangiography is not being performed in this study

Appendix I, "What will happen if I take part in this research study?"/Follow-Up (Text)

- 1st paragraph, 5th bullet: Chest x-ray added to be consistent with follow-up parameters described in the protocol
- 2nd paragraph: 6 months added due to an inadvertent omission
- 3rd and 4th paragraphs: Reversed for increased clarity
3rd paragraph (previously 4th paragraph): "persistent" simplified to "growing"; 12-week evaluation description (1st bullet) deleted due to redundancy with paragraph below; "spreading" simplified to "growing" (2nd bullet)

Appendix I, "What will happen if I take part in this research study?"/Follow-Up (Table)

- Within 42 days before starting study
  - 1st bullet: Clarified that biopsy is of tumor
  - 2nd bullet: Possible lymph node biopsy added to be consistent with follow-up parameters described in the protocol

- Week 5, last bullet: "1 blood test" changed to "blood test" for simplicity

- 8 weeks after the end of radiation therapy, 5th bullet: Chest x-ray added to be consistent with follow-up parameters described in the protocol

- 12 weeks after the end of radiation therapy
  - 3rd bullet: Clarified that scope is performed if recommended by the study doctor
  - Last bullet: "worse in the treated area" changed to "present" for increased accuracy

- 9, 12, 18, and 24 months after the end of radiation therapy
  - 6 months added due to an inadvertent omission
  - 3rd bullet: Clarified that scope is performed if recommended by the study doctor

Appendix II

- Superscript e: Moved from "at 8 weeks" to "at 12 weeks" for increased clarity and accuracy

- 2nd row: Weekly assessment of smoking/alcohol history deleted because this assessment is not needed on a weekly basis

- 5th row: Weekly assessment of anal/groin exam deleted because this assessment is not needed on a weekly basis

- 7th row: Colonoscopy added per modification in Section 3.1.2.2

- 9th row: Follow-up schedule for chest x-ray or CT or PET/CT changed from 12 weeks to 8 weeks because initial post-chemoradiation imaging should be performed at the 8-week follow-up. The 12-week imaging requirements were in error, as they would be duplicative.

- 10th row: Follow-up schedule for abdomen/pelvis CT or MRI or PET/CT changed from 8 weeks to 12 weeks because initial post-chemoradiation imaging should be performed at the 8-week follow-up. The 12-week imaging requirements were in error, as they would be duplicative.
• Last row: "Post-treatment" corrected to "post-treatment biopsy" due to an inadvertent omission

• Footnote h: 6 months added due to an inadvertent omission
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RTOG 0529 has been updated as follows:

Eligibility Checklist:

- Pages 1 and 2: Questions 12 and 24, originally written to be consistent with Sections 3.1.9 and 3.2.6.8, were combined into one question, #12, to reduce redundancy. Question 24 was deleted, and subsequent questions were appropriately renumbered.
- Page 3: Question 21, "Medical Oncologist's name", was added, as it was inadvertently omitted from this demographic portion of the checklist.

Section 12.1: The schedule for the Follow-up Form (F1) was revised to "Every 3 months from the start of RT" versus "from the end of RT". In addition, the schedule for the Post treatment Response Form (F2) was simplified to read, "Within 1 week of 8 and 12 week post-RT completion evaluations".

An updated protocol is available (no password required) on the RTOG Web site, www.rtog.org