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News Release

Embargoed until 2:15 pm ET, Monday, September 26, 2016

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Intermediate risk prostate cancer may be well controlled with brachytherapy alone

Initial report of large NRG Oncology/RTOG 0232 study demonstrates effectiveness of prostate brachytherapy as a stand-alone modality for progression free survival

BOSTON, September 26, 2016 -- For men with intermediate risk prostate cancer, radiation treatment with brachytherapy alone can result in similar cancer control with fewer long-term side effects, when compared to more aggressive treatment that combines brachytherapy with external beam therapy (EBT), according to research presented today at the 58th Annual Meeting the American Society for Radiation Oncology (ASTRO).

NRG Oncology/RTOG 0232 is a phase III, multi-institutional trial conducted at 68 cancer centers throughout the U.S. and Canada from 2003 to 2012 to assess whether adding EBT to transperineal interstitial permanent brachytherapy conveyed an additional benefit in progression free survival (PFS), or control of the cancer growth, at five years following treatment. Brachytherapy is a type of radiation therapy (RT) where radioactive seed implants are inserted directly into a patient's tissue to deliver treatment to the tumor while limiting radiation exposure for surrounding tissue.

Participants in the study included 588 men diagnosed with intermediate risk prostate cancer (i.e., clinical stage T1c-T2b) and enrolled in the trial between 2003 and 2012. Prostate cancer risk groups are assigned based on the prostate biopsy results, which include the Gleason score (GS) -- an indication of how aggressively the tumor cells may behave -- and the prostate specific antigen (PSA) level in the patient's blood at the time of diagnosis. Eligible patients for this trial had either a GS between two and six coupled with a PSA between 10 and 20; or a GS of 7 and a PSA less than 10.

Patients were randomized to one of two treatment arms, where 292 patients received brachytherapy alone (the B group) and 287 patients received 45 Gy partial EBT to the pelvic area in addition to brachytherapy (the EBT+B group). Brachytherapy treatment included the use of I-125 or Pd-103 (radioactive Iodine-125 or Palladium-103), prescribed to 110 Gy or 100 Gy respective boost dose for the patients who received brachytherapy plus EBT, and 145 Gy or 125 Gy respective dose for the patients who received brachytherapy alone. EBT was delivered by either intensity-modulated RT or three-dimensional conventional RT.

The primary outcome for this study, PFS, was estimated using the Kaplan-Meier method, and researchers compared the two treatment arms with two-sample binomial testing. Short-term/acute and long-term/late side effects also were measured, including both gastrointestinal (GI) and genitourinary (GU) toxicities. Treatment groups did not differ significantly on any baseline characteristics. The median participant age was 67, two-thirds of patients (67 percent) had stage T1 disease, and 89 percent fell in the GS 7/PSA < 10 group. Median follow-up for all patients was 6.7 years, and 443 patients were eligible for five-year follow-up analyses.

At five years following RT, survival rates for men who received brachytherapy alone were comparable to those who underwent more aggressive radiation treatment. The PFS rate at five years post-treatment was 85 percent for EBT+B patients and 86 percent for B patients (Hazard Ratio, HR, 1.02; futility $p = 0.0006$).

Although PFS rates were comparable between treatment groups, differences emerged in the rates of more serious side effects. Overall toxicity levels were similar across groups only for acute side effects (i.e., those that occur closely following treatment), with eight percent of patients in each cohort reporting acute grade 3+ side effects. Late severe toxicities were more common for EBT+B patients (12 percent) than for B patients (7 percent), as were severe GU side effects GU (7 vs. 3 percent) and severe GI toxicities (3 vs. 2 percent).

"These findings suggest that many men with intermediate risk prostate cancer can be well managed with seed implant alone and do not require the addition of external beam radiation," said Bradley Prestidge, MD, lead author of the study and Medical Director of the Bon Secours Cancer Institute at DePaul Medical Center in Norfolk, Virginia. "Contrary to expectations, the more aggressive, combined treatment did not result in superior cancer control rates at five years follow-up, indicating that men can achieve a similar survival benefit with fewer late side effects through brachytherapy alone."

The abstract, "Initial Report of NRG Oncology/RTOG 0232: A Phase III Study Comparing Combined External Beam Radiation and Transperineal Interstitial Permanent Brachytherapy with

Brachytherapy Alone for Selected Patients with Intermediate Risk Prostatic Carcinoma Identification and Validation of Intrinsic Subtypes of Prostate Cancer," will be presented in detail during a scientific session at ASTRO's 58th Annual Meeting at 2:15 p.m. Eastern time on Monday, September 26, 2016. To speak with Dr. Prestidge, please contact ASTRO's media relations team on-site at the Boston Convention and Exhibition Center on September 25-28, by phone at 703-286-1600 or by email at press@astro.org.

ATTRIBUTION TO THE AMERICAN SOCIETY OF RADIATION ONCOLOGY (ASTRO) ANNUAL MEETING REQUESTED IN ALL COVERAGE.

Full study abstract available on the final page of this release.

ABOUT ASTRO'S ANNUAL MEETING

ASTRO's 58th Annual Meeting, the nation's premier scientific meeting in radiation oncology, will be held September 25-28, 2016, at the Boston Convention and Exhibition Center in Boston. The 2016 Annual Meeting is expected to attract more than 11,000 attendees from across the globe, including oncologists from all disciplines and members of the entire radiation oncology team. Led by ASTRO president David C. Beyer, MD, FASTRO, the 2016 meeting will feature keynote addresses from Kathleen Sebelius, former U.S. Secretary of Health and Human Services; Thomas James Lynch Jr., MD, Chair and CEO, Massachusetts General Physicians Organization; and Jason Ragogna, general manager, SMS and Safety Alliances, Corporate Safety, Security, and Compliance, Delta Air Lines, Inc. The Presidential Symposium, "Prostate Cancer: Defining Value and Delivering It," highlights the meeting's theme of "Enhancing Value, Improving Outcomes" and will feature recent practice-changing studies and current developments in value-based care for prostate cancer. ASTRO's four-day scientific meeting will feature a record number of abstracts, including 368 oral presentations, 1,760 posters and 180 digital posters in more than 50 educational sessions and 20 scientific panels for 20 disease-site tracks. For more information about ASTRO's 58th Annual Meeting, visit www.astro.org/AnnualMeeting. For press registration and news briefing information for ASTRO's 58th Annual Meeting, visit www.astro.org/AMPress.

ABOUT ASTRO

ASTRO is the premier radiation oncology society in the world, with more than 10,000 members who are physicians, nurses, biologists, physicists, radiation therapists, dosimetrists and other health care professionals who specialize in treating patients with radiation therapies. As the leading organization in radiation oncology, the Society is dedicated to improving patient care through professional education and training, support for clinical practice and health policy standards, advancement of science and research, and advocacy. ASTRO publishes three medical journals, International Journal of Radiation Oncology • Biology • Physics (www.redjournal.org), Practical Radiation Oncology (www.practicalradonc.org) and Advances in Radiation Oncology (www.advancesradonc.org); developed and maintains an extensive patient website, RT Answers (www.rtanswers.org); and created the Radiation Oncology Institute (www.roinstitute.org), a nonprofit foundation to support research and education efforts around the world that enhance and confirm the critical role of radiation therapy in improving cancer treatment. To learn more about ASTRO, visit www.astro.org.

EMBARGOED UNTIL MONDAY, SEPTEMBER 26, 2016, 2:15 P.M. ET

Abstract ID: 7

ASTRO News Briefing: Advances in Prostate Cancer Care, Tuesday, September 27, 2016, 8:00 a.m. - 9:00 a.m. ET

Scientific Session: Monday, September 26, 2016, 2:15 p.m. - 3:45 p.m. ET

Initial Report of NRG Oncology/RTOG 0232: A Phase III Study Comparing Combined External Beam Radiation and Transperineal Interstitial Permanent Brachytherapy with Brachytherapy Alone for Selected Patients with Intermediate Risk Prostatic Carcinoma

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Purpose/Objective(s): To determine if combined external beam therapy (EBT) and transperineal interstitial permanent brachytherapy (B) results in better progression-free survival (PFS) at 5 years compared to B alone, among selected intermediate risk prostatic carcinoma patients (pts). This is the initial primary endpoint report.

Materials/Methods: Men with prostate cancer, clinical stage T1c-T2b and either Gleason Score (GS) 2-6/PSA 10-20 or GS 7/PSA <10 were eligible and randomized to receive either 45 Gy partial pelvis EBT and brachy (EBT+B) or B alone. EBT could be delivered by 3D or IMRT. B allowed the use of I-125 or Pd-103, prescribed to 110 Gy or 100 Gy boost dose respectively, in the EBT+B arm and 145 Gy or 125 Gy respectively, in the B arm. The study was designed to test for a 10% increase in 5-yr PFS for the EBT+B arm, with a 1-sided α of 0.025, 90% statistical power, & 5 interim analyses; requiring 586 pts. PFS (failure: ASTRO PSA, clinical, or death from any cause) was estimated by the Kaplan-Meier method and arms compared using a 2-sample binomial test. Protocol-specified interim efficacy and futility analyses were conducted and presented to an external Data Monitoring Committee (DMC). Efficacy testing used Haybittle-Peto at an α of 0.001 and futility was tested by reversing the null and alternative hypotheses at an α of 0.0001.

Results: Between June 2003 and February 2012, 588 men were randomized; 287 EBT+B and 292 B eligible, with median follow-up of 6.7 yrs. There were no significant differences in baseline characteristics between arms; median age 67, 89% had GS 7/PSA < 10, and 67% were T1. At the 5th interim analysis, of the required 443 pts with 5 yrs of follow-up, 5-yr PFS (95% CI) was 85% (80, 89) for the EBT+B arm and 86% (81, 90) for the B arm (HR=1.02, futility p=0.0006). Based on these futility results, the DMC recommended early release for the initial reporting of the primary endpoint. Acute overall ≥ grade 3 toxicity was similar, with 8% for EBT+B and 8% for B. Overall ≥ grade 3 late toxicity was 12% for EBT+B compared to 7% for B. Grade 3 or higher GU toxicity was 7% and 3%, while GI was 3% and 2% in the EBT+B and B arms, respectively. Analyses of secondary efficacy and other objectives are forthcoming.

Conclusion: Among men with intermediate risk prostate cancer in this study, the addition of external beam therapy to brachytherapy did not result in superior PFS compared to brachytherapy alone in this initial report. Toxicity in both groups was limited, but there were fewer late effects, mostly GU, noted in the brachytherapy alone arm.

Supported by NCI grants U10CA21661, U24CA81647, U10CA37422, U10CA180868, U10CA180822, U10CA10953, & U24CA180803