News Release

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Press Room in Atlanta
September 22-25
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Fewer weeks of hormone therapy before radiation treatment reduces side effects and yields comparable disease-specific-survival for intermediate risk prostate cancer patients

Atlanta, September 23, 2013 – A shorter course of androgen suppression therapy prior to radiation therapy, when compared to a longer course of androgen suppression therapy, yields favorable outcomes and fewer adverse effects for intermediate-risk prostate cancer patients, according to research presented today at the American Society for Radiation Oncology's (ASTRO) 55th Annual Meeting. The study confirmed a disease-specific-survival (DSS) rate of 95 percent when patients received fewer weeks of neoadjuvant (NEO) total androgen suppression (TAS).

The multi-institutional phase III trial, Radiation Therapy Oncology Group (RTOG) 9910, evaluated 1,490 intermediate-risk prostate cancer (PCa) patients from 152 institutions in the U.S. and Canada. Patients were accrued from 2000 to 2004 and followed for an average of 9 years, and the average age of the men was 71 at the time of accrual. The patients were stratified and randomized into two groups—Group 1 consisted of 752 patients who received eight weeks of NEO TAS, and Group 2 consisted of 738 patients who received 28 weeks of NEO TAS. Both groups then received eight weeks of external beam radiation therapy (RT) and concurrent TAS.

Cumulative incidence was used to estimate and test efficacy for DSS, prostate-specific antigen (PSA) failure, locoregional tumor progression and distant metastasis. Overall survival (OS) rates were

estimated via the Kaplan-Meier method and efficacy tested with log rank. There were 30 PCa deaths in Group 1, for a 10-year DSS rate of 95 percent; and 24 PCa deaths in Group 2, for a 10-year DSS rate of 96 percent (no statistical difference). There were 200 additional deaths not attributable to PCa in Group 1 for a 10-year OS rate of 66 percent, and 196 such deaths in Group 2, for a 10-year OS rate of 67 percent. By 10 years, 27 percent of patients had a PSA failure (using the newer RTOG-ASTRO definition of nadir+2), 5 percent had PCa recurrence in the prostate (locoregional) and 6 percent had distant metastasis. Hot flashes and erectile dysfunction were more common in Group 2.

"Sometimes, preliminary research leads us to assume that more treatment is better, but this study serves as a strong cautionary note to put the promising treatment to the test," said Thomas Pisansky, MD, lead author of the study and professor of radiation oncology at the Mayo Clinic in Rochester, Minn. "Overall, both groups had very, very good outcomes, but patients assigned to Group 2 had more side effects from androgen suppression than Group 1, who received only eight weeks of NEO TAS. Now, investigators know the upper boundary of how much androgen suppression is needed in this group of patients. The results have substantial importance because they can alter the research strategy to one in which investigation can now concentrate on ways to simplify the treatment and further reduce side effects."

The abstract, "Radiation Therapy Oncology Group 9910: Phase III Trial to Evaluate the Duration of Neoadjuvant (NEO) Total Androgen Suppression (TAS) and Radiation Therapy (RT) in Intermediate-Risk Prostate Cancer (PCa)," will be presented in detail during the Plenary session at ASTRO's 55th Annual Meeting at 2:00 p.m. Eastern time on September 23, 2013. To speak with Dr. Pisansky, contact Michelle Kirkwood on September 22-25, 2013, in the ASTRO Press Office at the Georgia World Congress Center in Atlanta at 404-222-5303 or 404-222-5304, or email michellek@astro.org.

ASTRO's 55th Annual Meeting, held in Atlanta, September 22-25, 2013, is the premier scientific meeting in radiation oncology and brings together more than 11,000 attendees including oncologists from all disciplines, medical physicists, dosimetrists, radiation therapists, radiation oncology nurses and nurse practitioners, biologists, physician assistants, practice administrators, industry

representatives and other health care professionals from around the world. The theme of the 2013 meeting is "Patients: Hope • Guide • Heal" and will focus on patient-centered care and the importance of the physician's role in improving patient-reported outcomes and the quality and safety of patient care. The four-day scientific meeting includes presentation of four plenary papers, 363 oral presentations, 1,460 posters and 144 digital posters in 70 educational sessions and scientific panels for 19 disease sites/tracks. Keynote and featured speakers include: William B. Munier, director of the Center for Quality Improvement and Patient Safety at the Agency for Healthcare Research and Quality; Darrell G. Kirch, MD, president and CEO of the Association of American Medical Colleges; James Cosgrove, PhD, director of the U.S. Government Accountability Office; Otis W. Brawley, MD, chief medical officer of the American Cancer Society; and Peter Friedl, MD, PhD, of St. Radboud University Nijmegen Medical Centre at the University of Nijmegen and MD Anderson Cancer Center.

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 that 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 two medical journals, International Journal of Radiation Oncology • Biology • Physics (www.redjournal.org) and Practical Radiation Oncology (www.practicalradonc.org); developed and maintains an extensive patient website, www.rtanswers.org; and created the Radiation Oncology Institute (www.roinstitute.org), a non-profit 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.

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2013 American Society for Radiation Oncology (ASTRO) 55th Annual Meeting
News Briefing, Monday, September 23, 2013, 8:30 a.m. Eastern time

Scientific Session: Monday, September 23, 2013, 2:00 – 3:10 p.m. ET, Georgia World Congress Center

1 Radiation Therapy Oncology Group 9910: Phase III Trial to Evaluate the Duration of Neoadjuvant (NEO) Total Androgen Suppression (TAS) and Radiation Therapy (RT) in Intermediate-Risk Prostate Cancer (PCa)

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Purpose/Objective(s): To determine primarily if extended duration NEO TAS followed by external RT + concurrent TAS improves disease-specific survival (DSS) compared to standard-duration NEO TAS, and secondarily effects on overall survival (OS), disease-free survival (DFS), clinical and biochemical relapse (BR), and adverse effects (AE).
Materials/Methods: Between February 2000 - May 2004, 152 institutions accrued 1579 patients with intermediate-risk PCa to a North American prospective trial. Patients were stratified and randomly assigned to TAS (luteinizing-hormone releasing-hormone analog + non-steroidal anti-androgen) of 8-week duration (Arm 1) or 28-week duration (Arm 2) prior to RT (prostate [70.2Gy/39 fractions] ± seminal vesicles ± pelvic nodes) + concurrent 8-week TAS. Assuming 8-year (yr) DSS of 79% (Arm 1), the trial required 270 PCa deaths to detect a 33% reduction in hazard of PCa death in Arm 2 with two-sided α=0.05 and 90% power. The first of 3 planned interim analyses was specified at 50 PCa deaths. Cumulative incidence estimated and tested efficacy for DSS, ASTRO-consensus (3-rises; 1997) BR and clinical relapse. OS and DFS (clinical relapse, BR or death) were estimated with Kaplan-Meier and efficacy tested using log rank. Arm 1 is reference for hazard ratio (HR). Time to event analysis is based on intent to treat and reported up to 10 yr.
Results: 1490 patients (Arm 1=752; Arm 2=738) were eligible with 8.7-yr median follow-up. Median age=71 yr, T1b-2=94%, Gleason >6= 73%, PSA >10=53%. There were 30 PCa deaths in Arm 1 (10-yr DSS=95%) and 24 in Arm 2 (96%); HR=0.81, p = 0.45. 200 additional deaths were not attributed to PCa or cause unknown in Arm 1 (10-yr OS=66%) with 196 in Arm 2 (67%); HR=0.95, p = 0.62. 10-yr DFS was 24% (Arm 1) *vs*. 23% (Arm 2), HR=0.96, p = 0.47. 10-yr cumulative incidence of BR in Arm 1 *vs*. Arm 2 was 57% *vs*. 60%, HR=1.01, p = 0.84; 10-yr local-regional relapse was 6% *vs*. 4%, HR=0.65, p = 0.07; 10-yr distant relapse was 6% *vs*. 6%, HR=1.07, p = 0.80. The late RT grade >2 AE incidence was 10% (Arm 1) *vs*. 8%; sexual grade >2 AE in 8% (Arm 1) *vs*. 17%.
Conclusions: Prior studies established short-term NEO TAS with RT + concurrent TAS as standard of care for patients with intermediate-risk PCa. This study confirmed high DSS and low clinical relapse risk through 10 years with this approach using moderate-dose RT. Although BR was common and DFS was low, this must be interpreted cautiously as the ASTRO (1997) definition does not account for androgen recovery. Extending NEO TAS >8 weeks and total TAS duration >16 weeks does not improve the endpoints herein for patients with intermediate-risk PCa as a whole.
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Author Disclosure Block: T.M. Pisansky: None. **D. Hunt:** None. **L.G. Gomella:** None. **M.B. Amin:** G. Consultant; Executive Advisory Board - Foundation Medicine, Amgen, Inc. **A.G. Balogh:** None. **D.M. Chinn:** None. **M. Seider:** None. **M. Duclos:** None. **S.A. Rosenthal:** None. **H.M. Sandler:** G. Consultant; Astellas Pharma, Inc.