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The addition of 24 months of daily anti-androgen therapy during and after radiation therapy significantly improves long-term overall survival following prostate cancer recurrence after a radical prostatectomy.

10-year follow up of RTOG 9601 also shows lower incidence of prostate cancer-related death without increase of toxicity

San Antonio, October 19, 2015—Prostate cancer patients who face recurrence after radical prostatectomy (RP) have better overall survival rates with a combination of salvage radiation therapy (RT) and 24 months of anti-androgen therapy (AAT) than with RT alone, according to research presented today at the American Society for Radiation Oncology’s (ASTRO’s) 57th Annual Meeting.

Many men with prostate cancer who undergo RP—surgical removal of the prostate—experience recurrence, as evidenced by an elevated prostate specific antigen (PSA) level. These patients are then often given salvage RT to the prostate tumor bed. Androgens are male hormones that can stimulate the growth of prostate cancer cells, therefore, peripheral androgen blockage, or
AAT, can be used to decrease or suppress the amount of androgens in the body in combination with salvage RT to possibly improve patient survival in this setting.

RTOG 9601 was a large phase III double-blinded, placebo-controlled trial that evaluated if long-term AAT, when combined with salvage RT, would improve OS and other cancer control outcomes for prostate cancer patients who had failed RP. Conducted from 1998 to 2003, the study included 761 prostate cancer patients from centers across the U.S. and Canada and compared a salvage regimen of only RT to one of RT plus AAT.

The study group included patients had undergone a RP—and had, or had developed elevated prostate specific antigen (PSA) levels from 0.2 to 4.0 ng/ml with prostate tumors classified as either T2pN0 and a positive surgical margin (indicating the tumor was confined to the prostate with no lymph nodes affected) or T3pN0 (indicating the tumor had grown outside of the prostate, but no lymph nodes were affected).

The patients were randomly assigned to receive either RT of 64.6 Gy in 36 fractions of 1.8 Gy plus 24 months of AAT therapy of 150 mg of daily bicalutamide during and after RT; or to receive the RT regimen plus a placebo. A total of 384 patients were assigned to the RT plus AAT group, and 377 patients were assigned to the RT plus placebo group.

With a median follow-up of 12.6 years, the study results showed that the actuarial OS at 10 years was 82 percent for the RT plus AAT patients and 78 percent for the RT plus placebo patients; with a hazard ratio of 0.75 (95 percent CI: 0.58-0.98) with a two-sided p-value = 0.036.

Data indicated that the addition of AAT decreased the rate of death by prostate cancer and decreased the risk of the cancer metastasizing (spreading to other parts of the body). The 12-year incidence of prostate cancer central-reviewed deaths was 2.3 percent for the RT plus AAT group, compared to 7.5 percent for the RT plus placebo group (p<0.001). At 12 years, the cancer had metastasized in 51 patients (14 percent) in the RT plus AAT group, compared to 83 patients (23 percent) in the RT plus placebo group (p<0.001).
Additionally, late grade 3 and grade 4 bladder and bowel side effects were similar in both groups, whereas 70 percent of men in the RT plus AAT group reported swelling of the breasts, compared to 11 percent from the RT plus placebo group.

“Over the last 25 years, many men with intermediate risk prostate cancer have undergone RP, yet many will face recurrence in one to four years with a rising PSA,” said lead study author William U. Shipley, MD, FACP, FASTRO, Andres Soriano Distinguished Professor of Radiation Oncology at the Massachusetts General Hospital and the Harvard Medical School. “Our results show that salvage RT plus androgen blockage, when compared to RT with a placebo, improved long-term overall survival and reduced death from prostate cancer without adding significantly to radiation toxicity. Because prostate cancer progresses slowly, follow-up of over 12 years was necessary to demonstrate a statistically better patient survival with combined AAT and RT therapy. Further statistical analyses, which are underway, may identify subgroups of prostate cancer patients who may not benefit from hormone therapy added to salvage RT, and others for whom it may be especially beneficial.”

The abstract, “Report of NRG Oncology/RTOG 9601, a phase III trial in prostate cancer: Anti-androgen therapy (AAT) with bicalutamide during and after radiation therapy (RT) in patients following radical prostatectomy (RP) with pT2-3pN0 disease and an elevated PSA,” will be presented in detail during the Plenary session at ASTRO’s 57th Annual Meeting at 2:15 p.m. Central time on Monday, October 19, 2015. To speak with Dr. Shipley, please call Nancy Mayes in ASTRO’s Press Office at the Henry B. González Convention Center, in San Antonio on October 18 – 21, 2015 at 210-258-8104 or 210-258-8105, or email press@astro.org.

ASTRO’s 57th Annual Meeting, being held at the Henry B. González Convention Center in San Antonio, October 18-21, 2015, is the nation’s premier scientific meeting in radiation oncology. The 2015 Annual Meeting is expected to attract 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. Led by ASTRO President Bruce D. Minsky, MD, FASTRO, a radiation oncologist specializing in gastrointestinal cancers, Professor of
Radiation Oncology, and the Frank T. McGraw Memorial Chair at The University of Texas MD Anderson Cancer Center, Houston, the theme of the 2015 Meeting is “Technology Meets Patient Care.” Dr. Minsky’s Presidential Symposium, “Multidisciplinary Management of Esophageal and Rectal Cancers,” will feature Leonard L. Gunderson, MD, MS, FASTRO, and Joel E. Tepper, MD, FASTRO, to highlight imaging, staging, genomics and data mining approaches, as well as the latest advances in esophageal and colorectal cancer treatment. ASTRO’s four-day scientific meeting includes presentation of more than 2,100 abstracts: five plenary papers, 351 oral presentations, 1,609 posters and 171 digital posters in more than 53 educational sessions and 26 scientific panels for 20 disease-site tracks. Three keynote speakers will address a range of topics including cancer biology in radiation oncology, the essential roles of a physician, and patient safety: Arul Chinnaiyan, MD, PhD, Professor and Director, Michigan Center for Translational Pathology; Francisco G. Cigarroa, MD, Past President and Chancellor, University of Texas; and Gerald B. Hickson, MD, Senior Vice President and Assistant Vice Chancellor, Vanderbilt University Medical 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 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, 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.
LBA5 Report of NRG Oncology/RTOG 9601, a phase III trial in prostate cancer: Anti-androgen therapy (AAT) with bicalutamide during and after radiation therapy (RT) in patients following radical prostatectomy (RP) with pT2-3pN0 disease and an elevated PSA

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Purpose/Objectives: To test if long term AAT when combined with RT in patients with prostate cancer (PC) will improve overall survival and other cancer control outcomes.

Materials/Methods: Post-RP patients with pT3pN0 or with pT2pN0 (and also positive margins) who had or developed elevated PSA levels from 0.2 to 4.0 ng/ml were randomized on a phase III, double-blinded, placebo-controlled trial of RT + placebo (64.8 Gy in 36 fractions of 1.8 Gy) vs RT + AAT (24 months of bicalutamide, 150mg daily) or placebo during and after RT. The primary end-point is overall survival. The trial design required 725 patients and provided 80% power to detect a reduction in death rate by at least 28.5% and a 1-sided significance level of 0.046.

Results: From 3/98 to 3/03, 761 eligible patients (median age 65) were randomized to RT + AAT (384) or RT + placebo (377). 248 patients (33%) were pT2pN0 and 513 patients (67%) were pT3pN0. 671 patients (88%) had a PSA nadir after RP of < 0.5 ng/ml. 649 patients (85%) had an entry PSA value of <1.6, 112 patients (15%) had an entry PSA of 1.6-4. Median follow up was 12.6 years. The actuarial overall survival at 10 years was 82% for RT plus AAT and 78% for RT + placebo and a hazard ratio of 0.75 (95% CI: 0.58-0.98) with a 1-sided p-value of 0.018 (2-sided p-value = 0.036). PSA progression was defined as a PSA > 0.5 ng/ml in patients whose treatment resulted in an undetectable PSA or, if not, when the PSA rose 0.3 ng/ml above the entry PSA. Freedom from PSA Progression (FFP) estimated at 10 years was 46% for RT + AAT and 30% for RT + placebo (p < 0.001). The 12-year incidences of PC central-reviewed deaths were 2.3% for RT + AAT and 7.5% for RT + placebo (p<0.001). The cumulative incidence of metastatic PC at 12 years was less in the RT + AAT arm, 14% (51 patients), vs 23% (83 patients) in the RT + placebo arm (p<0.001). Late Grade III and Grade IV toxicity were similar in the AAT and placebo arms. By category the combined Grade III plus Grade IV toxicities for RT +AAT and RT +placebo were: for bladder 7.0% vs 6.7%, bowel 2.7% vs 1.6%. Gynecomastia (mostly all Grades I and II) differed significantly by treatment arm, 70% and 11%. In the RT +AAT arm Grade III was the highest liver toxicity observed which occurred in <1% of patients.

Conclusion: The addition of 24 months of AAT with 150mg daily of bicalutamide during and after RT significantly improved the long term overall survival and FFP and reduced the incidence of metastatic PC and PC death without adding significantly to radiation toxicity. Supported by NCI grants U10CA21661, U10CA180868, U10CA180822, and U10CA37422 and AstraZeneca. NCT Trial #NCT00002874.