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Press Office in San Francisco
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Long-term androgen deprivation (LTAD) therapy combined with high-dose radiation therapy (HDRT) for prostate cancer improves biochemical control and survival rates

San Francisco, September 15, 2014— Prostate cancer patients who receive high-dose radiation therapy (HDRT) followed by a longer period of hormone suppression therapy, or androgen deprivation therapy (ADT), have higher five-year biochemical, disease-free survival (bDFS) and overall survival rates compared to patients who receive HDRT and a shorter duration of ADT, according to research presented today at the American Society for Radiation Oncology's (ASTRO's) 56th Annual Meeting.

Because prostate cancer cells typically require androgen hormones such as testosterone to grow, ADT is often recommended for patients with prostate cancer. Radiation therapy (RT) combined with ADT is an established, standard of care for patients with locally advanced prostate cancer.

This multi-center study evaluated whether HDRT combined with long-term androgen deprivation (LTAD) therapy for 28 months was associated with better patient outcomes compared to HDRT combined with short-term ADT (STAD) for four months.

Between 2006 and 2010, 362 patients were enrolled in the study at 9 cancer centers in Spain, and 355 patients met all study criteria. The patients had cT1c – T3aN0M0 prostate cancer (with no lymph node

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involvement and no metastases and unfavorable risk factors), and prostate specific antigen (PSA) levels of less than 100 ng/ml.

All patients received four months of neoadjuvant and concomitant ADT + HDRT, meaning the ADT was simultaneous to the RT treatment and began prior to radiation in an attempt to reduce tumor size. The median RT dose to the prostate was 78 Gy.

Patients were then randomly assigned to two groups: 177 patients received adjuvant Goserelin (a luteinizing hormone that suppresses production of testosterone) subcutaneously for 24 additional months to form the LTAD group; the remaining 178 patients received only four months of ADT and were categorized as the STAD group. A comparable number of intermediate risk (IR) patients and high-risk (HR) patients were assigned to each group. There were 166 IR patients (85 in the LTAD group; 81 in the STAD group), and 189 HR patients (92 in the LTAD group; 97 in the STAD group).

The study's primary endpoints were bDFS and toxicity scores (radiation-related side effects). The bDFS rate with prostate cancer is based upon the measurement of a patient's PSA level. If a patient's PSA level does not rise upon post-treatment follow-up evaluations, the patient is considered to not be in biochemical failure, or does not have biochemical disease—meaning the cancer is considered to be ablated and not growing or spreading.

A total of 11 patients in the LTAD group and 15 patients in the STAD group had bDFS, according to Phoenix Consensus definition ($p=0.003$).

After a median follow-up of 63 months, the five-year bDFS was significantly higher in the LTAD group (89.8 percent, compared to the STAD group (81.3 percent) ($p=0.019$).

The study also evaluated metastasis free survival (MFS) and overall survival (OS). The five-year MFS was also significantly higher for the LTAD group—93.6 percent compared to 83.4 percent in the STAD group ($p=0.009$). There was also a significant benefit in the OS for patients treated with LTAD (94.8 percent) versus STAD (86.1 percent, $p=0.009$), this benefit being more evident in patients with high-risk prostate cancer ($p=0.010$). Radiation-related side effects of \geq Grade 2 were acceptably low and not significantly different in both groups.

“The management of patients with intermediate- and high-risk prostate cancer is highly challenging,” said lead study author Almudena Zapatero, MD, PhD, a radiation oncologist at Hospital Universitario de la Princesa in Madrid Spain. “The clinician must choose the type of local treatment as well as the optimal timing

and sequence of hormone therapy. Moreover, rapid and ongoing advances in treatment options require that physicians consider options that can impact both survival and quality-of-life. The five-year results of our study show that the combination of high-dose external radiotherapy utilizing new technologies, such as IMRT, VAMT and IGRT, and 28 months of hormone therapy are a very successful combination to achieve positive prostate cancer control. Of paramount consideration, LTAD therapy in combination with HDRT provides good quality of life through a non-invasive, safe and efficient treatment approach for patients with high-risk prostate cancer.”

The abstract, “Randomized Phase III Trial of Adjuvant Androgen Deprivation in Combination with High-dose Conformal Radiotherapy in Intermediate and High Risk Localized Prostate Cancer,” will be presented in detail, with updated results, during the plenary session at ASTRO’s 56th Annual Meeting at 2:15 p.m. Pacific time on Monday, September 15, 2014. To speak with Dr. Zapatero, please call Michelle Kirkwood on September 14 – 17, 2014, in the ASTRO Press Office at San Francisco’s Moscone Center at 415-978-3503 or 415-978-3504, or email michellek@astro.org.

ASTRO’s 56th Annual Meeting, to be held at the Moscone Center in San Francisco, September 14-17, 2014, is the nation’s premier scientific meeting in radiation oncology. The 2014 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 G. Haffty, MD, FASTRO, a radiation oncologist specializing in breast cancer, the theme of the 2014 Meeting is “Targeting Cancer: Technology and Biology,” and the Presidential Symposium, “Local-regional Management of Breast Cancer: A Changing Paradigm,” will feature Jay R. Harris, MD, FASTRO, and Thomas A. Buchholz, MD, FASTRO, to highlight recent practice-changing, landmark studies and current developments in the local-regional management of breast cancer. ASTRO’s four-day scientific meeting includes presentation of up to four plenary papers, 360 oral presentations, 1,862 posters and 144 digital posters in more than 50 educational sessions and scientific panels for 20 disease-site tracks. Three keynote speakers will address a range of topics including oncologic imaging, biology and targeting in oncology, and human error and safety concerns: Hedvig Hricak, MD, PhD, Chair of the Department of Radiology and the Carroll and Milton Petrie Chair at Memorial Sloan Kettering Cancer Center; Frank McCormick, PhD, FRS, DSc (hon), Professor Emeritus and the David A. Wood Distinguished Professor of

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Tumor Biology and Cancer Research of the University of California at San Francisco Helen Diller Family Comprehensive Cancer Center; and Sidney Dekker, PhD, MA, MSc, Professor and Director of the Safety Science Innovation Lab at Griffith University, Brisbane, Australia.

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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2014 American Society for Radiation Oncology (ASTRO) 56th Annual Meeting
News Briefing, Monday, September 15, 2014, 8:15 a.m. Pacific time

Plenary Session: Monday, September 15, 2014, 2:15 – 3:25 p.m. PT, the Moscone Center

PL-02 **Randomized Phase III Trial of Adjuvant Androgen Deprivation in Combination with High-dose Conformal Radiotherapy in Intermediate and High Risk Localized Prostate Cancer**

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Purpose/Objective(s): Although androgen deprivation (AD) combined with radiotherapy significantly decreases mortality of patients with locally advanced prostate cancer (PCa), controversy remains about the optimal duration of AD associated with dose escalation RT. This trial was designed to evaluate whether long-term AD (LTAD) improves outcome compared to short-term AD (STAD) in patients treated with high-dose radiotherapy (HDRT).

Materials/Methods: Between 2006 and 2010, 362 assessable patients were enrolled. Eligibility included patients with cT1c-T3aN0M0 PCa with intermediate and high risk factors according to NCCN criteria and PSA less than 100 ng/ml. All patients received 4 months of neoadjuvant and concomitant AD (STAD) + HDRT (median dose to the prostate 78.0 Gy) before randomization to adjuvant gosereline (LTAD) for two years. Stratification was performed according to risk group (intermediate risk [IR] versus high risk [HR]). Primary endpoints were biochemical-disease free survival (bDFS) and toxicity scores. Secondary endpoints included metastasis free survival (MFS), overall survival (OS) and cancer specific survival (CSS).

Results: Three hundred and fifty two patients (STAD =177, LTAD=175) were eligible with 57 months median follow-up. There were 188 HR patients (STAD = 97, LTAD = 91) and 164 IR patients (STAD = 80, LTAD = 84) (p=0.669). Twenty-three patients in the STAD group and 7 patients in the LTAD group had biochemical failure according to Phoenix Consensus definition (p=0.003). At 5 years bDFS was significantly improved in the LTAD group (95.4%, 95% CI: 93.2-97.6, compared to the STAD group (86.1%%, 95% CI: 83.5-88.7). Five-year MFS was 85.5% (95% CI: 82.9-88.1) for STAD and 93.2% (95% CI: 91.0-95.4) for LTAD, and OS was 88.8% (95% CI: 86.3-91.3) for STAD and 94.0% (95% CI: 91.9-96.1) for LTAD. Grade ≥ 2 radiation related adverse effects in both groups were not significantly different.

Conclusions: This study shows that the combination of LTAD plus HDRT provides superior bDFS compared with STAD + HDRT. Further follow-up is needed to confirm these findings and to estimate precisely the impact on OS and CSS.

Author Disclosure Block: A. Zapatero: None. A. Guerrero: None. J. Maldonado: None. A. Alvarez: None. C. Gonzalez San Segundo: None. M. Cabeza Rodriguez: None. V. Macias: None. A. Pedro-Olive: None. F. Casas: None. A. Boladeras: None. C. Martin de Vidales: None. M. Vazquez de la Torre: None. F.A. Calvo: None.