The Randomized NRG Oncology RTOG 9601 Protocol Reports That Men With Prostate Cancer Who Have a PSA Recurrence Following Radical Prostatectomy Have Improved Survival With the Addition to Salvage Radiotherapy of a Long-term Course of Antandrogen Therapy Compared With Salvage Radiotherapy Alone

SAN ANTONIO—It is well established that a rising serum prostate-specific antigen (PSA) level is an indication of cancer progression in men diagnosed with prostate cancer and treated with radical prostatectomy (RP). For these patients, adding 24 months of anti-androgen therapy (AAT) during and after salvage radiotherapy (RT) improves overall survival statistically compared with treating them with salvage RT alone, according to the long-term results of a clinical trial conducted by the Radiation Therapy Oncology Group (RTOG), now conducting research as NRG Oncology. The RTOG 9601 study results presented today at the plenary session of the 57th Annual Meeting of the American Society for Radiation Oncology (ASTRO) also reveal that the addition of ATT to salvage RT reduces prostate cancer death and the development of metastatic prostate cancer without increasing radiation toxicity.

“Over the last 25 years, many men with intermediate-risk prostate cancer have undergone RP, yet many will face recurrence subsequently with a rising PSA,” says lead author William U. Shipley, M.D., FACP, FASTRO, who is the Andres Soriano Distinguished Professor of Radiation Oncology at the Massachusetts General Hospital and the Harvard Medical School, both in Boston. “Our results show that salvage RT plus peripheral androgen blockade (AAT with bicalutamide), when compared with RT plus 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.” With a median follow-up now of 12.6 years, the study results showed the actuarial overall survival at 10 years was 82 percent for the RT plus AAT arm and 78 percent for the RT plus placebo arm (P = 0.036). The 12-year incidence of prostate cancer-related deaths was 2.3 percent for the RT plus AAT arm, compared with 7.5 percent for the RT plus placebo arm. At 12 years, the cancer had metastasized in 51 patients (14 percent) in the RT plus AAT arm, compared with in 83 patients (23 percent) in the RT plus placebo arm. Additionally, late bladder and bowel toxicity were low and similar in both groups, whereas 70 percent of men in the RT plus AAT arm reported swelling of the breasts, compared with 11 percent in the RT plus placebo arm.

Conducted at sites across the United States and Canada from 1998 to 2003, the RTOG 9601 trial enrolled 761 men with prostate cancer who had undergone RP and subsequently developed elevated PSA levels. The patients were randomized to receive either salvage RT plus placebo (377 patients) or salvage RT plus AAT (384 patients).
“Further statistical analyses, which are underway, may identify subgroups of patients who may not benefit from hormone therapy added to salvage RT and other subgroups for whom it may be especially beneficial. “Also, because anti-androgen therapy, which suppresses testosterone production, is now used more commonly than peripheral androgen blockade with AAT, its use should be evaluated,” says Shipley in regard to next research steps for the population of post-RP patients referred for salvage RT. Shipley also emphasizes the clinical researchers’ gratitude for the willingness of the patients to participate on this and other randomized trials and for the essential role they play in advancing cancer care.

“The results of this trial are testament to the importance of phase III randomized controlled trials for determining significant benefits. Congratulations to the trial team for their commitment to obtaining the quality of research data necessary for impacting the clinical care of patients with prostate cancer,” says Walter J. Curran Jr., M.D., an NRG Oncology Group Chairman and Executive Director of the Winship Cancer Institute of Emory University in Atlanta.

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