ADT and Chemotherapy Added to ART Improves FFP Post-Prostatectomy

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Although clinical data suggest that the use of adjuvant radiation therapy (ART) following radical prostatectomy benefits both progression-free and overall survival [Chin JL. *Can Urol Assoc J.* 2009], subgroups with adverse pathologic findings have been identified at high risk for treatment failure despite both surgery and ART. Although systemic therapies such as docetaxel and androgen deprivation therapy (ADT) have been demonstrated to be effective treatments for men with metastatic prostate cancer, the effect of combining systemic therapy with ART had not been investigated in this high-risk group. Mark Hurwitz, MD, Jefferson Medical College of Thomas Jefferson University, Philadelphia, Pennsylvania, USA, reported results from RTOG 0621: Adjuvant 3DCRT/IMRT in Combination With Androgen Suppression and Docetaxel for High Risk Prostate Cancer Patients Post-Prostatectomy: A Phase II Trial [NCT00528866].

The primary objective of the trial was to assess whether the addition of ADT and docetaxel to ART for patients at high risk for failure with ART alone could improve 3-year freedom from progression (FFP). Patients eligible for the trial were those who had been found in a prior randomized trial, SWOG 8794, to have a 50% risk for failure by 3 years despite radiation. Specifically, this group had either a postprostatectomy prostate-specific antigen (PSA) nadir >0.2 ng/mL and a Gleason score ≥7 or a PSA nadir ≤0.2 ng/ml but a Gleason score ≥8 and a tumor that had displayed extracapsular extension.

A total of 80 patients were enrolled, resulting in 74 analyzable patients. Notably, patients enrolled tended to have more risk factors than in the historical control series, with >80% of patients having Gleason scores ≥8, more than half with seminal vesicle (SV) involvement, and nearly half with PSA >0.2 ng/mL. The study schema involved all 80 patients receiving 6 months of ADT with luteinizing hormone-releasing hormone agonists and either flutamide or bicalutamide. External-beam radiation began 8 weeks after the initiation of androgen suppression, followed 3 to 6 weeks later by the application of 6 21-day cycles of docetaxel. In terms of the ART, there was an initial dose of radiation to the pelvic field of 4500 cGy, followed by boost of a minimum 5040 cGy to the prostatic fossa and SV remnants, and a final boost of 6660 cGy to the prostatic fossa. Although both 3D conformal radiation therapy and intensity-modulated radiation therapy (IMRT) were allowed, 80% of patients received IMRT.

The primary end point was 3-year FFP, with failure defined as PSA ≥0.4 ng/mL to allow comparison with historical controls from SWOG 8794. The reported 3-year FFP was 73.0% (95% CI, 62.9 to 83.1), compared with a projected 50% rate. The predominant initial failure was biochemical. With median follow-up of 4.4 years, 11 patients experienced distant metastasis, and there were 2 prostate cancer-specific deaths. In terms of adverse events, Dr Hurwitz noted that rates of febrile neutropenia and infection were consistent with other reported series of docetaxel for prostate cancer and that no significant increase in long-term toxicity from the use of ADT, chemotherapy, and ART was seen, characterizing the rates of gastrointestinal and genitourinary toxicities as acceptable.

In conclusion, Dr Hurwitz reiterated that the addition of ADT and docetaxel chemotherapy to ART following prostatectomy for men at high risk for failure with ART alone resulted in >20% improvement in 3-year FFP compared with historical controls. Dr Hurwitz continued that in light of the findings presented, phase 3 trials assessing use of ADT and chemotherapy with ART in patients in the high-risk population are warranted.

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