Letter to the Editor


Salvage Radiotherapy and Hormone Therapy: Change Is Coming, Just Not Quite Yet

Drs. Ghadjar and Wiegel bring up excellent points regarding the use of molecular imaging in the context of salvage radiotherapy (SRT), the potential benefits of dose-escalated SRT, and the use of targeted radiotherapy to all metastatic sites without androgen deprivation therapy (ADT). These ideas may translate into improved outcomes for patients with recurrent prostate cancer. However, the framework put forth by our multidisciplinary group on when to initiate hormone therapy with SRT was built upon level 1 evidence [1]. There are no long-term data or reported randomized data to demonstrate that any of the strategies suggested by Drs. Ghadjar and Wiegel will improve clinically meaningful endpoints, such as metastasis-free survival, prostate cancer-specific survival, or overall survival. This prevents us from providing formalized recommendations regarding these exciting approaches. Fortunately, multiple ongoing and completed randomized phase 2 and 3 trials are going to test these hypotheses.

As Drs. Ghadjar and Wiegel outlined, multiple studies have nicely demonstrated that molecular imaging can readily identify positron emission tomography (PET)–avid sites of disease outside of standard radiotherapy fields in men with recurrent prostate cancer [2]. Unfortunately, PET has a limit of detection of 2–4 mm and is unable to identify micrometastatic disease. Given that the most common site of recurrence after surgery is local, prostate bed radiotherapy should not be omitted at this time. Therefore, the knowledge that molecular imaging provides does not immediately alter our recommended treatment paradigm on the use of ADT with SRT, but may in the future impact extended radiotherapy field design with the increasing widespread use of molecular imaging.

Moreover, despite our enthusiasm for Drs. Ghadjar and Wiegel's proposed changes to the current standard of care, we must remain cautious about their true potential benefit and value. In RTOG 9601, a trial of often late SRT in unfavorable-risk prostate cancer (67% T3 disease; 75% positive margins), only 5.8% of men died of prostate cancer at 12 yr in the combined SRT + ADT arm [3]. Demonstration of further improvements in prostate cancer–specific survival in the context of a randomized trial will be challenging. It is more plausible that the changes proposed by Drs. Ghadjar and Wiegel would impact quality of life more than long-term survival outcomes. This could be achieved by either a reduction in the use or duration of ADT, or by potentially avoiding futile pelvic radiotherapy in men with bona fide distant metastatic disease.

It will take a unified prostate cancer community to pursue these research efforts to open and enroll in large, practice-changing trials to allow us to answer whether any of these advances can improve the quality or quantity of a man’s life. Other exciting avenues for men with recurrent prostate cancer include the use of predictive biomarkers to guide therapy. NRG GU-006 will be the first randomized phase 2 predictive biomarker stratified trial in recurrent prostate cancer to test if a biomarker can identify which men among those treated with primarily early SRT might derive the most benefit from next-generation androgen therapy. The culmination of these many exciting areas of research will hopefully one day change the standard of care.

Conflicts of interest: Daniel E. Spratt is supported by a Prostate Cancer Foundation Young Investigator Award (DES) and has served on an advisory board for Dendreon. Felix Y. Feng has served on advisory boards for Medivation/Astellas, Genome Dx, Nanostring, Celgene, and Dendreon, and has received grant funding from Varian, Medivation/Astellas, and Celgene.

References


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October 6, 2017