

Response to 20-17583 Lancet_Letter_Ghadjar

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Advances in radiotherapy techniques have reduced treatment-related morbidity. Patients having salvage radiotherapy in RADICALS-RT(1) may have been more likely to receive IMRT than those having adjuvant treatment. However, this does not alter our conclusion that salvage radiotherapy should be the current standard of care. Indeed, one advantage of a salvage radiotherapy policy is that delaying treatment means that patients may benefit from any further developments in radiotherapy technique.

The optimum dose of prostate bed radiotherapy after radical prostatectomy has not been well studied. A dose of 60-64Gy was used in the older adjuvant trials,(2, 3) largely because of the technical limitations when those trials were designed prior to the widespread use of three-dimensional conformal treatment planning. The RADICALS-RT dose of 66Gy was based on a survey of investigators, is widely practiced internationally and accords with current guidelines. It is true that both lowering the dose of radiotherapy, and omitting androgen deprivation, would be expected to reduce toxicity. However, given that adjuvant radiotherapy did not improve disease control in RADICALS-RT or GETUG-AFU 17,(4) this would not alter our conclusion that salvage radiotherapy should be the current standard.

We strongly agree that longer follow-up of RADICALS-RT and GETUG-AFU 17, as well as RAVES,(5) will be important in order to study longer-term, clinically meaningful endpoints including freedom from distant metastasis and cause-specific survival. Combining the planned long-term analyses is part of the ARTISTIC meta-analysis work.(6) However, based on the current data from these trials, we maintain that a policy of salvage radiotherapy should be the current standard, pending the results of longer term analyses.

It is not known which patients, if any, benefit from adjuvant radiotherapy. The evidence cited by Ghadjar and Wiegel should be regarded as hypothesis-generating, either because it was based on an observational study,(7) or, because in the EORTC 22911 trial, early salvage radiotherapy for PSA failure was not mandated.(8) The ARTISTIC meta-analysis (6) included 1729 patients with a calculable CAPRA-S score, of whom 609 (35%) had a score ≥ 6 , indicating a $>50\%$ risk of recurrence after surgery.(9) However, there was no evidence that any effect of adjuvant radiotherapy on event-free survival varied according to any of the predefined subgroups.

A policy of salvage radiotherapy after radical prostatectomy has the considerable advantage that it avoids the need for radiotherapy in those men who are effectively cured by surgery alone. This policy should be the current standard-of-care and can be revisited if further data emerge showing adjuvant radiotherapy does more good than harm.

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