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“ Times to local and distant progression were significantly longer in men who received immediate therapy ”

How to treat men with a rising serum PSA level after radical prostatectomy is a much-discussed topic in urology. Two randomized phase III trials, recently published in *The Lancet Oncology*, provide some much-needed data on this pressing clinical issue with regards to giving androgen deprivation therapy (ADT) to these patients.

Duchesne and colleagues conducted the Timing Of Androgen Deprivation (TOAD) trial in 29 oncology centres in Australia, New Zealand and Canada to assess whether giving immediate ADT improves overall survival compared with delaying ADT until therapy is indicated. Participants were randomly assigned in a 1:1 ratio to receive either immediate or delayed therapy and in total, 293 men were recruited to this study.

The primary end point in this investigation was overall survival and secondary end points included time to clinical progression and global quality of life for the first 2 years. Luteinizing hormone-releasing hormone agonist monotherapy was prescribed to 79% of the men who received ADT.

Overall survival at 5, 6 and 7 years was 86.4%, 76.4% and 65.5%,

respectively, for men who received delayed ADT, compared with 91.2%, 85.6% and 81.0%, respectively, for those who had immediate ADT. Of those men who were recruited as they had experienced a PSA level relapse, 19% in the delayed ADT group died compared with 11% in the immediate ADT group, and estimated 5-year overall survival was 78.2% and 84.3%, respectively. Times to local and distant progression were significantly longer in men who received immediate therapy.

Adverse events were experienced by 78% of men in the immediate therapy group compared with 47% of men in the delayed therapy group, with 41% and 32% of men in the immediate or delayed arm, respectively, having a grade 4 adverse event. Quality-of-life questionnaire scores decreased for men in both groups, by 6% in the immediate therapy (considered clinically important) arm and by 3% in the delayed therapy arm (considered clinically trivial).

Carrie and co-workers investigated the effects giving salvage radiotherapy with or without short-term ADT in men with a rising PSA level after radical prostatectomy in the GETUG-AFU 16 trial.

In total, 742 patients enrolled at 43 centres in France were included in the intention-to-treat analysis, 373 in the radiotherapy alone group and 369 in the radiotherapy plus ADT arm. Patients who received ADT were given an injection of goserelin on their first day of irradiation and a second goserelin injection 3 months later. The primary end point for this trial was progression-free survival (PFS) and secondary end points included overall survival, late toxicities and changes in quality of life.

Patients who received ADT with salvage radiotherapy were significantly more likely to be clinically or biochemically progression free 5 years after treatment than those who had radiotherapy alone, and they did not experience additional late adverse events: 5-year PFS was 80% for the radiotherapy plus ADT group and 62% in the radiotherapy alone group. Subgroup analysis of patients with low-risk or high-risk disease revealed 5-year PFS was 75% and 58%, respectively, in the radiotherapy alone group and 87% and 77% in the radiotherapy plus ADT group. However, 5-year overall survival did not differ between groups.

Quality-of-life questionnaire scores did not significantly differ between treatment groups at 1 year or 5 years after treatment.

The data from both these trials provides clinicians with much-needed information regarding treatment options in the setting of men with rising a PSA level after radical prostatectomy.

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**ORIGINAL ARTICLES** Duchesne, G. M. et al. Timing of androgen-deprivation therapy in patients with prostate cancer with a rising PSA (TROG 03.06 and VCOG PR 01-03 [TOAD]): a randomised, multicentre, non-blinded, phase 3 trial. *Lancet Oncol.* [http://dx.doi.org/10.1016/S1470-2045\(16\)00107-8](http://dx.doi.org/10.1016/S1470-2045(16)00107-8) (2016) | Carrie, C. et al. Salvage radiotherapy with or without short-term hormone therapy for rising prostate-specific antigen concentration after radical prostatectomy (GETUG-AFU 16): a randomised, multicentre, open-label phase 3 trial. *Lancet Oncol.* [http://dx.doi.org/10.1016/S1470-2045\(16\)00111-X](http://dx.doi.org/10.1016/S1470-2045(16)00111-X) (2016)