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EDITORIAL

Be gentle with ideas but harsh on facts

The research giant in prostate cancer research Donald Coffey has been quoted as stating: 'Be gentle with ideas but harsh on facts'. This proverbial saying comes to mind when reading the systematic review and meta-analysis of short-term and long-term neoadjuvant androgen deprivation therapy (ADT) prior to radical prostatectomy by Satoshi Katayama *et al* in this issue of the Journal. In their review, the authors selected as primary endpoints biochemical recurrence free survival, metastasis free survival, and overall survival and their secondary endpoints were surgical margins, organ-confined disease, and pathologic complete response. It appears that the authors have a strong conviction that neoadjuvant ADT provides advantages in selected patients. The authors conclude from their meta-analysis that the use of long-term neoadjuvant ADT provides a significant benefit in terms of the secondary endpoints pathologic outcomes compared to short-term ADT and further state that 'given that the favorable trend in an increased rate of pathologic complete response, long-term neoadjuvant ADT prior to RP has the potential to improve patient outcomes'. They then must admit: 'however, due to the lack of available RCTs to properly investigate survival benefits in patients with PC receiving long-term neoadjuvant ADT, neoadjuvant ADT should not be used outside the clinical trial due to the considerable risk of adverse events'.

There is a disconnect between these two statements, the first statement is basically an idea, the second statement is a fact. To make this clear, the authors focus on secondary endpoints and the positive results that has been observed for these. The authors then argue that the reason why this has not led to increased survival is that studies to date have not had survival as primary endpoint, had too short follow-up, or that cases were heterogeneous. Despite the lack of a documented increase in survival, the authors argue that a multimodal therapy including neoadjuvant ADT is needed, with the advent of novel androgen receptor targeted (ART) therapies. However, since ART:s were not studied in this meta-analysis, no conclusions about them can be made.

Further data against the authors arguments include a previous Cochrane review and meta-analysis in which neoadjuvant ADT offered no survival benefit for men undergoing radical prostatectomy [1,2].

In the introduction the references used are vaguely associated with the text, the authors state that 'with the increasing role of radical prostatectomy in advanced and oligometastatic PC, neoadjuvant ADT has received renewed attention as adjunct treatment' [3–5]. However, the references report on cytoreductive radical prostatectomy in metastatic prostate cancer and very little in these articles are about ADT. The same could be seen when the author describes the side effects of ADT, the referred articles are for men with metastatic disease and these men could probably tolerate more complications than men in a curative setting [6,7].

Men who have positive surgical margins and detectable PSA after radical prostatectomy benefit from postoperative external beam radiotherapy given adjuvant or as salvage RT and signs of adverse disease may be masked by neoadjuvant ADT and the opportunity of secondary curative treatment can be missed [8].

It is obvious that the authors are convinced that neoadjuvant ADT prior to RP is beneficial, and when the evidence is lacking to support their view, they extrapolate results from other settings to be applied for these men. The authors beliefs and hope for better treatment options are laudable but treatment recommendations must be supported by facts not ideas. To date there is no convincing data that neoadjuvant ADT in conjunction with radical prostatectomy increases survival as shown by this meta-analysis.

In conclusion, until convincing data are available to support the use of neoadjuvant ADT prior to radical prostatectomy, clinicians should refrain from using this treatment outside of clinical trials.

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