

### Re: Extended Versus Limited Lymph Node Dissection in Bladder Cancer Patients Undergoing Radical Cystectomy: Survival Results from a Prospective, Randomized Trial

Gschwend JE, Heck MM, Lehmann J, et al

Eur Urol. 2019;75:604–11

#### Experts' summary:

This multicenter, nationwide, randomized trial investigated the impact of extended (eLND) versus limited lymph node dissection on recurrence-free survival (RFS) in invasive ( $\geq T1$ ) bladder cancer (BC). There was no significant difference in the primary endpoint, although a trend towards superior outcomes from eLND was noted [1].

#### Experts' comments:

The results of this study were keenly awaited for many years to clarify the prognostic role of eLND at RC. However, urologists are still confronted with the same questions this study intended to answer. It has to be stated that randomized studies on critical topics in BC surgery are difficult to conduct, for many reasons. Therefore, the authors should be commended for their efforts. Nonetheless, some results deserve further discussion.

Although the accrual period lasted from 2006 to 2010, the study results were published some 8 yr later. This is surprising given the fact that RFS was the primary endpoint. As the median time to recurrence after RC is approximately 12 mo [2], the results should have been mature enough for publication years ago. So what was the reason for the delay?

One reason might be the primary endpoint itself, which was defined as a 15% benefit in RFS for eLND. Admittedly, this level is ambitious and even questionable, as patients with T1 disease (12–16% in both arms) were eligible for inclusion, a group of patients with a risk of <10% of lymph node-positive disease [2,3]. With regard to the study design, the authors refer to Leissner et al. [4]. However, in this study the mean lymph node yield was almost 30% higher for eLND. So a question inevitably arises about the meticulousness of lymph node sampling and processing during the study period.

Strikingly, given the fact that only experienced surgeons were considered for the study, the rate of positive margins was relatively high (8–9%) in both groups, a finding that might have diminished any long-term benefit of eLND since the majority of patients with positive margins usually experience recurrence very early after RC [3].

So, is this a “negative” study on the prognostic benefit of eLND and should we refrain from performing eLND at RC in

the future? The answer is a definitive “no”. The subanalysis on the role of adjuvant chemotherapy reveals that the detection of positive lymph nodes translates into beneficial postoperative treatment decisions. Thus, the “diagnostic” benefit of eLND becomes “therapeutic” regardless of the primary endpoint analysis. This study also unravels another “myth” with regard to the morbidity of eLND: eLND did not result in higher complication rates per se, as has been claimed by a number of retrospective series and surgeons in the past [3].

In summary, given the inadequacy of the current radiological modalities for reliable detection of regional lymphatic spread in muscle-invasive BC (MIBC) [5], the standard of diagnostic care should be eLND, as this will allow more MIBC patients to be considered for (hopefully curative) adjuvant systemic treatment modalities.

**Conflicts of interest:** The author has nothing to disclose.

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### Re: Pembrolizumab plus Axitinib versus Sunitinib for Advanced Renal-Cell Carcinoma

Rini BI, Plimack ER, Stus V, et al

N Engl J Med. 2019;380:1116–27

#### Experts' summary:

An open-label, phase 3 trial was performed in patients with previously untreated advanced clear-cell renal cell carcinoma

(RCC) to receive pembrolizumab (200 mg) plus axitinib (5 mg) or sunitinib (50 mg). The primary endpoints were overall survival (OS) and progression-free survival (PFS) in the intention-to-treat population. The main secondary endpoint was the objective response rate. Treatment with pembrolizumab plus axitinib resulted in significantly longer OS and PFS and a higher objective response rate when compared to treatment with sunitinib.