



## Letter to the Editor

**Re: Richard J. Sylvester, Willem Oosterlinck. An Immediate Instillation after Transurethral Resection of Bladder Tumor in Non-Muscle-Invasive Bladder Cancer: Has the Evidence Changed? Eur Urol 2009;56:43–5**

Today, the European Association of Urology (EAU) guidelines recommend early instillation for all patients with non-muscle-invasive bladder cancer (NMIBC) [1]; however, no randomized prospective study exists that clearly substantiates this recommendation for intermediate and high-risk tumours.

Presently, two published studies report on the value of early instillation in addition to series of chemotherapy [2,3]. Both studies fail to show any clear benefit for early treatment when maintenance treatment was given. Merging two randomized studies, Boufflioux and co-workers demonstrated similar recurrence curves for early treatment and maintenance compared to delayed treatment and maintenance instillations [2]. Similarly, in the study by Hendricksen et al, no difference in time to recurrence was demonstrated when early instillation (within 48 h) was added to subsequent instillations with epirubicin [3].

One published study so far has investigated the value of early instillation in addition to bacillus Calmette-Guérin (BCG) treatment [4]. In this study ( $n = 161$ ), 57% of patients in the early instillation group had no recurrence compared to 51% in the BCG-only group ( $p = 0.095$ ). Although it has been pointed out that the study is underpowered, it is debatable whether such a small benefit would be clinically significant.

In a recent editorial, Sylvester and Oosterlinck [5] argue for immediate instillation in all patients with NMIBC after transurethral resection of the bladder, despite recent published data [6] suggesting that such treatment only benefits low-risk patients. It should be kept in mind that the evidence for early instillation is based on a meta-analysis that included 1476 patients, of which only 10.8% (163 patients) had recurrent tumour at inclusion and 15.7% (237 patients) had more than one tumour. In the multiple-tumour group, a separate analysis could only be conducted in 7.5% (111) of the patients, and although a trend in favour of early treatment was seen in this group of patients, it was not significant ( $p = 0.06$ ). No separate analysis was

published on recurrent tumours [7]. Consequently, the recent study [6] in which 104 recurrent and 117 multiple cases could be assessed adds substantially to the current knowledge on early instillation.

The inefficacy of early instillation that was found in these two subgroups is difficult to dismiss. In their editorial, Sylvester and Oosterlinck state that the effect in intermediate and high-risk tumours might be diluted due to long follow-up [5]. However, despite possible underpowering and dilution of data, the clinical efficacy in terms of numbers needed to treat (NNT) in intermediate and high-risk tumours seems to be too high in these patients to support such treatment. One should also keep in mind that 28% of patients originally included were excluded due to such factors as muscle-invasive tumours or a benign pathology report, further increasing the NNT [6]. Because 50% of recurrent tumours can be fulgurated in the office under local anaesthesia [8], our interpretation of the available literature is that such treatment cannot be recommended until there is sufficient evidence supporting a clinically significant effect.

**Conflicts of interest:** The authors have nothing to disclose.

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