Letter to the Editor

An immediate, single instillation of mitomycin C in non-muscle invasive bladder cancer: can we define which patients do and do not benefit?

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We thank the author for his interest in our recent article in which we have re-analysed the data of our previous large randomised trial regarding the value of an immediate instillation of mitomycin C (1).

The value of an immediate instillation with chemotherapy after transurethral resection of non-muscle-invasive bladder cancer (NMIBC) has been a topic of debate for decades (2-4). Currently, the European Association of Urology (EAU) guidelines recommend an immediate instillation for low-risk tumours. For intermediate risk tumours, an immediate instillation is only recommended in patients with a previous low recurrence rate (less than or equal to one recurrence per year) and expected European Organisation for Research and Treatment of Cancer (EORTC) recurrence score of less than five (5). The basis for these recommendations is a meta-analysis conducted by Sylvester *et al.* in which an immediate instillation did not seem to benefit these two patient groups (4).

In our original randomised controlled trial we found that an immediate instillation of mitomycin C (MMC) significantly reduces the risk of recurrence in patients with NMIBC (6). The recurrence risk was reduced from 36% (95% confidence interval, 33–39%) to 27% (95% confidence interval, 24–30%) after 3 years of follow-up. This corresponds to a number needed to treat of twelve. However, the risk groups and adjuvant instillation schedules in that study differ from the currently used risk groups and recommended adjuvant therapies (5). These differences made it hard to compare our results to those of a meta-analysis conducted by Sylvester *et al.* (4). Therefore, we re-analysed our data after reclassifying patients into the currently used risk groups and by using the data regarding previous recurrence rate and calculated EORTC risk scores.

We found that the effect of an immediate instillation of MMC did not differ from other risk groups in patients with a high recurrence rate or higher EORTC risk scores (7). These findings demonstrate that an immediate instillation with MMC reduces the risk of recurrence in all patients with NMIBC, irrespective of EORTC recurrence score or previous recurrence rate. Based on these findings, we believe that patients should not be withheld an immediate instillation after transurethral resection based on either of these criteria.

The author states that the timing of an immediate instillation in our original trial was not defined (1). Although the exact timing was not registered, the study protocol indicated that the immediate instillation had to be administered within 24 hours after transurethral resection of the tumour. Whether an instillation given within the first few hours after transurethral resection is more effective cannot be answered from our data (8). Although several trials have demonstrated the value of an immediate instillation, it seems that the search for a subgroup of patients that will not benefit from an immediate instillation

continues. In our opinion the focus should be on patients with high risk tumours that will be treated with Bacillus Calmette-Guérin (BCG) instillations. The literature on the value of an immediate instillation in this group is scarce and therefore no solid conclusions on the effect of an immediate, single instillation in these groups can be drawn.

In our original trial, we also included patients with high risk tumours, and found no difference regarding the effect of an immediate instillation in this group. However, at that time patients were treated with adjuvant schedules of MMC instead of the current standard BCG. Therefore, the question whether an immediate instillation is effective prior to BCG instillations remains unanswered.

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None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

References

1. Batura D. Redefining the role of immediate intravesical instillation of mitomycin C in non-muscle invasive bladder cancer. Transl Androl Urol 2018;7:S729-31.
2. Berrum-Svennung I, Granfors T, Jahnson S, et al. A single instillation of epirubicin after transurethral resection of bladder tumors prevents only small recurrences. J Urol 2008;179:101-5; discussion 105-6.
3. Brausi MA. Challenging the EAU guidelines regarding early repeat transurethral resection. Eur Urol Suppl 2011;10:5.
4. Sylvester RJ, Oosterlinck W, Holmang S, et al. Systematic Review and Individual Patient Data Meta-analysis of Randomized Trials Comparing a Single Immediate Instillation of Chemotherapy After Transurethral Resection with Transurethral Resection Alone in Patients with Stage pTa-pT1 Urothelial Carcinoma of the Bladder: Which Patients Benefit from the Instillation? Eur Urol 2016;69:231-44.
5. Babjuk M, Bohle A, Burger M, et al. EAU Guidelines on Non-Muscle-invasive Urothelial Carcinoma of the Bladder: Update 2016. Eur Urol 2017;71:447-61.
6. Bosschieter J, Nieuwenhuijzen JA, van Ginkel T, et al. Value of an Immediate Intravesical Instillation of Mitomycin C in Patients with Non-muscle-invasive Bladder Cancer: A Prospective Multicentre Randomised Study in 2243 patients. Eur Urol 2018;73:226-32.
7. Bosschieter J, Nieuwenhuijzen JA, Vis AN, et al. An immediate, single intravesical instillation of mitomycin C is of benefit in patients with non-muscle-invasive bladder cancer irrespective of prognostic risk groups. Urol Oncol 2018;36:400.e7-14.
8. Bosschieter J, van Moorselaar RJA, Vis AN, et al. The effect of timing of an immediate instillation of mitomycin C after transurethral resection in 941 patients with non-muscle-invasive bladder cancer. BJU Int 2018;122:571-5.

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