and sharing of follow-up modalities and chronology among specialists, whereby general practitioners, cardiologists, and endocrinologists are regularly informed of any need to adapt comorbidity treatments. We must keep in mind that short-term ADT is recommended for intermediate-risk PCa and long-term ADT for high-risk PCa in the case of external irradiation [1,2]; adjuvant ADT for patients with positive pelvic lymph nodes after surgery [3]; and intermittent instead of continuous ADT for metastatic PCa with a good initial response to ADT [4]. Clinicians should advise patients during follow-up to maintain the hope that new medical options could be available should relapse occur.

**Conflicts of interest:** The author is an advisor to Janssen and Janssen and receives lecture fees from Astra-Zeneca.

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**Reference:**


**Experts’ comments:**

This is a significant trial in a large multicenter setting that assessed an important clinical question for a common urologic presentation. The study was designed to assess the clinical effectiveness of MET rather than therapeutic efficacy; therefore, radiological assessment was not a primary endpoint for participants.

However, closer inspection of the outcomes reveals that a potentially important trend may have been overlooked. Although the rates of stone clearance were similar among the tamsulosin (84.5%), nifedipine (86.3%) and placebo (86.3%) groups for calculi ≤5 mm, the differences were more pronounced for stones >5 mm, favoring tamsulosin (71.3%, 61.7%, and 60.6%, respectively). In addition, only 24.8% of calculi in the study were >5 mm and the majority of patients (75.2%) had calculi ≤5 mm.

Some clinicians believe that active treatment may not be necessary for stones ≤5 mm. Furthermore, many consider stone-free status after intervention as the presence of residual fragments ≤4 mm, and it is estimated that 95% of stones ≤4 mm pass within 40 d [2,3]. It could be argued that MET may be beneficial only for larger stones (>5 mm). Therefore, given that only 25% of the study participants had calculi >5 mm, the trial may have been underpowered for detection of a clinically significant difference for larger stones, as acknowledged by the authors. Overall, the potential benefits of MET may have been diluted by inclusion of smaller stones in this study. Similarly, a weak trend favoring MET was observed for distal ureteric stones (86.7% vs 82.1%).

Although the initial study protocol that was published indicated that participants would be asked to record whether they completed the full course of medical therapy in the 4-wk questionnaire, this was not conveyed in the final trial analysis [4]. The lack of verification of compliance with trial medications could undermine MET effects. This is particularly important for asymptomatic stones, for which patients are unlikely to remain compliant for the duration of the trial. In addition, only 94 patients in the tamsulosin arm had stones >5 mm. Noncompliance in this smaller cohort would have a greater impact on the results, and theoretically the 10.6%
difference observed between the tamsulosin and placebo arms is also influenced by the lack of MET adherence, further undermining the statistical power of this comparison.

Pain reported using a single self-reported questionnaire at 4 wk may not adequately capture potential analgesic benefits of MET, and the statement by the authors that there was no evidence that the drugs reduced pain does not sufficiently address the potential limitations of this assessment method.

The study also does not report the exact indications for intervention or whether the indications for such interventions differed among the three trial arms, or if interventions were more likely to succeed in any particular study arm.

Overall, there are a number of factors that should be considered by clinicians when deciding on MET effectiveness, and for some this trial may not completely dismiss all potential advantages of MET, at least not for all stone sizes and locations.

Conflicts of interest: The authors have nothing to disclose.

References


