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0302-2838/Published by Elsevier B.V. on behalf of European Association
of Urology.

<https://doi.org/10.1016/j.eururo.2022.01.016>



Re: Radical Cystectomy Against Intravesical BCG for High-Risk High-Grade Nonmuscle Invasive Bladder Cancer: Results From the Randomized Controlled BRAVO-Feasibility Study

Catto JWF, Gordon K, Collinson M, et al

J Clin Oncol 2021;39:202–14

Experts' summary:

The aim of the BRAVO study was to assess the feasibility of a randomized controlled trial (RCT) comparing intravesical bacillus Calmette-Guérin (BCG) maintenance instillations and radical cystectomy (RC) in high-risk, high-grade non-muscle-invasive bladder cancer (HRNMIBC). Of the 407 patients screened, 185 were eligible and approached. Of these, 50 consenting participants with HRNMIBC were randomly assigned (1:1). In the BCG arm, 92% received maintenance instillations and two patients developed metastatic bladder cancer (BC). In the RC arm, 80% underwent RC, of whom 10% had muscle-invasive BC. All of the participants were free of cancer at the end of the study. Quality of life was broadly similar in the two arms at 12 mo. The BRAVO study underlines the challenge in recruiting patients to such a clinical trial, bearing in mind the risk of undertreatment and overtreatment in HRNMIBC.

Experts' comments:

European guidelines suggest RC for selected patients with NMIBC [1]. The results of the BRAVO study were eagerly awaited in the search for a high level of evidence regarding the superiority of RC over BCG for some borderline NMIBCs. Theoretically, the scientific question raised by the BRAVO trial was excellent, but it collapsed on the possibility of recruiting patients in the field. As previously shown, notably in the treatment of prostate cancer [2], patients requiring surgery are not likely to be randomized. In fact, in RCTs comparing surgery to another treatment, there is a considerable attrition rate between the number of potentially recruitable patients and the number of patients who ultimately agree to participate in the study. Therefore, in the era of evidence-based medicine (EBM), the usual trial configuration in which patients are randomly assigned to treatment A or treatment B does not seem applicable to all fields of scientific research, especially surgery.

An outstanding example is the POUT trial, which showed the superiority of platinum-based chemotherapy after nephroureterectomy in upper tract urothelial carcinoma [3]. However, in contrast to the BRAVO study, the randomization took place after surgery in the POUT trial. Despite being a very well-designed clinical trial, the BRAVO study confronts us with the limits of application of EBM in surgery.

Today, we must admit that recruiting patients to RCTs comparing surgery to nonsurgical treatment can be extremely difficult, as shown by the BRAVO study. Surgeons should probably think outside the box and try to move forward with single-arm prospective trials recording perioperative morbidity and quality-of-life data to improve surgical techniques and patient care, rather than RCTs.

Conflicts of interest: The authors have nothing to disclose.

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<https://doi.org/10.1016/j.eururo.2022.01.011>

