

## Re: Robot-assisted Radical Cystectomy Versus Open Radical Cystectomy in Patients with Bladder Cancer (RAZOR): An Open-label, Randomised, Phase 3, Non-inferiority Trial

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### Experts' summary:

The RAZOR trial is the first randomised (1:1) phase 3 study assessing cancer control for both surgical approaches. The primary objective of this noninferiority trial was to compare 2-yr progression-free survival (PFS) among patients with radical treatment for bladder cancer. Between 2011 and 2014, 159 and 153 patients were included in the intention-to-treat analysis and underwent robot-assisted (RARC) and open radical cystectomy (ORC), respectively. All urinary diversions were extracorporeal. Patients were randomly allocated by institutions ( $n = 15$ ) and stratified by urinary diversion type, cT stage and Eastern Cooperative Oncology Group performance status. Surgeons who participated in the study were required to have performed at least ten RARC or ORC procedures in the year before the study. A noninferiority margin of  $-15\%$  points was considered on the basis of previous trials in colon and rectal cancers comparing open to minimally invasive surgery. Baseline characteristics were similar between the groups, and 2-yr PFS was 72.3% in the RARC versus 71.6% in the ORC arm, showing noninferiority of RARC to ORC (0.7% difference, 95% confidence interval  $-9.6\%$  to  $10.9\%$ ;  $p = 0.90$ ). PFS was worse for positive surgical margins (PSMs) or higher pT stage, with no significant differences between treatment groups.

### Experts' comments:

The European Association of Urology guidelines [1] support robotic surgery for radical cystectomy on the basis of previous feasibility trials showing evidence of lower estimated blood loss and transfusion rates and shorter hospital stays against longer operative time for RARC compared to ORC [2,3]. Previous trials focused on perioperative and functional outcomes. However, oncological outcomes had not yet been assessed in a randomised controlled trial for radical cystectomy. The RAZOR trial proves noninferior PFS at 2 yr for patients undergoing RARC, with no differences in secondary outcomes (overall and high-grade complications, PSM rates, and quality of life according to a patient-reported outcome measure). The 2-yr PFS outcome measure was selected on the basis of studies revealing correlation of more frequent bladder cancer recurrence at 2 yr with outcomes in longer studies [4].

Concerns with regard to minimally invasive surgery include recurrence at uncommon locations due to tumor seeding (eg, port site, peritoneal carcinomatosis), the PSM rate (tactile feedback), the extent of lymphadenectomy, and costs [5]. This study reported no port site recurrence, similar

local recurrence (3% vs 4%;  $p = 0.54$ ) and similar distant metastases rates. No differences were found for the mean number of lymph nodes removed (23.3 vs 25.7;  $p = 0.13$ ) or the PSM rate (6% vs 5%;  $p = 0.59$ ). Noninferior cancer control was proved, with no differences in complication rates.

The results have to be interpreted with caution because of some limitations. We have to consider selection bias since experienced surgeons performing all the surgeries, with some performing both RARC and ORC. Although equally balanced, the use of neoadjuvant chemotherapy and the extent of the lymph node dissection was left to the surgeon's discretion, introducing differences in disease management in a study evaluating cancer control. Another limitation is that cost data were not collected from all sites, as this was specified as a secondary outcome in the protocol. Evidence supported by expert consensus [1,6] proves that higher costs for RARC lead to noninferior oncologic and morbidity outcomes. The RAZOR trial results should encourage investigators to plan superiority trials for bladder cancer managed surgically.

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

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