



# READ IT BEFORE YOUR PATIENTS

## Bladder

### Chemoradiotherapy in muscle-invasive bladder cancer (BC2001): 10-years follow-up of a phase III randomised controlled trial.

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#### BACKGROUND

BC2001, the largest randomised trial of bladder-sparing treatment for muscle-invasive bladder cancer (MIBC), demonstrated improvement in locoregional control by adding fluorouracil and mitomycin C to radiotherapy (James ND, Hussain SA, Hall E, et al. Radiotherapy with or without chemotherapy in muscle-invasive bladder cancer. *N Engl J Med* 2012;366:1477-88). There are limited data on long-term recurrence risk.

#### OBJECTIVE

To determine whether benefit of adding chemotherapy to radiotherapy for MIBC is maintained in the long term.

#### DESIGN, SETTING, AND PARTICIPANTS

A phase III randomised controlled 2 × 2 factorial trial was conducted. Between 2001 and 2008, 458 patients with T2-T4a N0M0 MIBC were enrolled; 360 were randomised to radiotherapy (178) or chemoradiotherapy (182), and 218 were randomised to standard whole-bladder radiotherapy (108) or reduced high-dose-volume radiotherapy (111). The median follow-up time was 9.9 years. The trial is registered (ISRCTN68324339).

#### INTERVENTION

Radiotherapy: 55 Gy in 20 fractions over four weeks or 64 Gy in 32 fractions over 6.5 weeks; concurrent chemotherapy: 5-fluorouracil and mitomycin C.

#### OUTCOME MEASUREMENTS AND STATISTICAL ANALYSIS

Locoregional control (primary endpoint), invasive locoregional control, toxicity, rate of salvage cystectomy, disease-free survival (DFS), metastasis-free survival (MFS), bladder cancer-specific survival (BCSS), and overall survival. Cox regression was used. The analysis of efficacy outcomes was by intention to treat.

#### RESULTS AND LIMITATIONS

Chemoradiotherapy improved locoregional control (hazard ratio [HR] 0.61 [95% confidence interval {CI}] 0.43-0.86,  $p = 0.004$ ) and invasive locoregional control (HR 0.55 [95% CI 0.36-0.84],  $p = 0.006$ ). This benefit translated, albeit nonsignificantly, for disease-related outcomes: DFS (HR 0.78 [95% CI 0.60-1.02],  $p = 0.069$ ), MFS (HR 0.78, [95% CI 0.58-1.05],  $p = 0.089$ ), overall survival (HR = 0.88 [95% CI 0.69-1.13],  $p = 0.3$ ), and BCSS (HR 0.79 [95% CI 0.59-1.06],  $p = 0.11$ ). The five-years cystectomy rate was 14% (95% CI 9-21%) with chemoradiotherapy versus 22% (95% CI 16-31%) with radiotherapy alone (HR 0.54, [95% CI 0.31-0.95],  $p = 0.034$ ). No differences were seen between standard and reduced high-dose-volume radiotherapy.

## CONCLUSIONS

Long-term findings confirm the benefit of adding concomitant 5-fluorouracil and mitomycin C to radiotherapy for MIBC.

## PATIENT SUMMARY

We looked at long-term outcomes of a phase III clinical trial testing radiotherapy with or without chemotherapy for patients with invasive bladder cancer. We concluded that the benefit of adding chemotherapy to radiotherapy was maintained over 10 years.

