

BLADDER CANCER

Could chemohyperthermia finally set the NMIBC world on fire?

Chemohyperthermia (CHT) is safe and effective for the treatment of patients with intermediate-risk and high-risk non-muscle-invasive bladder cancer (NMIBC), according to a recent study published in *European Urology*.

Despite much research, treatment options for NMIBC remain limited. Intravesical therapy with mitomycin C (MMC) and BCG immunotherapy are widely used, but few major changes in adjuvant treatment have occurred. Chemotherapy combined with radiofrequency-induced hyperthermia has been in use for many years, with a randomized trial published in 2003 showing that CHT was more effective than MMC alone. Since then, some further data have shown reduced recurrence rates, but a lack of prospective data and other limitations of study design mean that it has been difficult to draw meaningful conclusions.

Arends and colleagues randomized 190 patients to receive 1 year of CHT (six weekly treatments and six maintenance treatments) or 1 year of BCG therapy (six weekly treatments and three weekly maintenance treatments at 3, 6 and 12 months). The study's primary end point was

24-month recurrence-free survival (RFS) in the intention-to-treat (ITT) and per-protocol analyses in all patients with papillary NMIBC ($n = 147$).

24-month RFS in the ITT analysis was 78.1% in patients who received CHT, compared with 64.8% in the BCG group ($P = 0.08$). Per-protocol analyses also reflected this result, showing a 24-month RFS of 81.8% in the CHT group and 64.8% in the BCG-treated patients ($P = 0.02$). Adverse events, which were recorded at every treatment or follow-up visit, did not identify any new safety concerns with CHT therapy; 1,540 CHT treatments were given to 90 patients and 1,431 adverse events were observed, mostly bladder spasm and bladder pain during treatment and dysuria, nocturia, and frequency after treatment. The most prevalent adverse effects in patients who had received BCG therapy were urinary frequency, dysuria, nocturia, haematuria, and fatigue, with 1,525 adverse events recorded in 1,923 treatments given to 94 patients.

These results suggest that CHT could be a good treatment option for patients with NMIBC, which



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could be particularly valuable in the current era of BCG shortages. Although they represent the first prospective data available on CHT in NMIBC, the results reflect other studies and the authors' clinical experience: "I don't find these results surprising," corresponding author J. Alfred Witjes told *Nature Reviews Urology*. "I have 16 years of experience with CHT and know it is very effective. It would be most useful for patients with highly recurrent NMIBC and high-risk and BCG failures, and emphasizes that there is more than just BCG for high-risk patients."

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ORIGINAL ARTICLE Arends, T.J. et al. Results of a randomised controlled trial comparing intravesical chemohyperthermia with mitomycin C versus Bacillus Calmette-Guérin for adjuvant treatment of patients with intermediate- and high-risk non-muscle-invasive bladder cancer. *Eur. Urol.* <http://dx.doi.org/10.1016/j.eururo.2016.01.006> (2016)