

Chemohyperthermia Shows Promise in Nonmuscle Bladder Cancer

Kate Johnson | March 30, 2015

MADRID — Chemohyperthermia, which combines bladder heating with intravesical chemotherapy, is more effective in the treatment of intermediate- to high-risk nonmuscle-invasive bladder cancer than traditional therapy with bacillus Calmette–Guérin (BCG), according to the first randomized phase 3 trial of the combined therapy.

"We think we could offer this more often to this group of patients, especially with the recent worldwide shortages of BCG, which have resulted in an additional treatment dilemma," said study investigator Tom Arends, MD, from the Radboud University Nijmegen Medical Center in the Netherlands.

The findings were presented here at the European Association of Urology 30th Annual Congress.

Data from the study were called "hot, new, and really important" by Brant Inman, MD, from Duke University Medical Center in Durham, North Carolina, who was not involved in the study.

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"This trial must be repeated in the United States, and soon," he told *Medscape Medical News*. "It is a very important trial for patients who want to minimize cancer recurrences and maximize the chance that they will keep their bladders once diagnosed with bladder cancer."

"With a larger study done over a shorter accrual time interval and a longer follow-up, I think we are very likely to find a new standard of care," he said.

In their study, Dr Arends and his team used the Synergo device, from Medical Enterprises, to heat the bladder wall to 42 °C.

The 142 patients, recruited from 11 centers in Europe and Israel from 2002 to 2012, were randomized to one of two treatments for a period of 12 months.

In the chemohyperthermia group, patients received six weekly treatments of bladder heating followed by the intravesical instillation of mitomycin 20 mg and six maintenance treatments.

In the BCG group, patients received 6 weekly treatments of BCG and 9 maintenance treatments.

On intention-to-treat analysis, recurrence-free survival at 24 months — the primary end point — was better in the chemohyperthermia group than in the BCG group (80.0% vs 66.0%; $P = .0694$). On per protocol analysis, the difference in the primary end point reached statistical significance (89.5% vs 71.0%; $P = .008$).

The difference in the rate of metastasis between the chemohyperthermia than BCG groups was not significant (1.7% vs 2.8%).

Chemohyperthermia Trumps BCG

"This study demonstrates, for the first time in a randomized trial, that chemohypertherapy may be better than BCG. To my knowledge, this is only the second randomized controlled trial for any form of chemohypertherapy for bladder cancer," said Dr Inman. The first was conducted in Italy more than a decade ago (*J Clin Oncol*. 2003;21:4270-4276).

Dr Inman was involved in the first North American trial of the experimental therapy, which had encouraging results and demonstrated that the procedure was well tolerated (*Int J Hyperthermia*. 2014;30:171-175).

However, the device used in that pilot study — the BSD-2000 hyperthermia system from BSD Medical — cost \$500,000. It is approved by the US Food and Drug Administration (FDA) for the treatment of cervical cancer, but its use is "not generalizable to the broader urologic community," he told *Medscape Medical News*.

In fact, the main barrier to this therapy in the United States is the fact that no bladder-heating device has been approved by the FDA.

Dr Inman said he is working with Combat Medical, which manufactures the COMBAT BRS system in Europe, to get such a device. "We hope to have it at Duke within months for initial testing and future trials," he said.

The COMBAT device is much less expensive, at about \$5000. "If it is as good as the very expensive alternatives — and preliminarily we think it is — we will have a low-cost way of delivering chemohyperthermia to the broader bladder cancer population," he explained.

With the novel immunotherapies on the horizon for bladder cancer showing promise, chemohyperthermia "would be a nice platform for combination therapy, since it is known to provoke immune responses through the release of heat shock proteins," Dr Inman said.

The trial was funded by Medical Enterprises, the manufacturer of the Synergo device. Dr Arends and Dr Inman have disclosed no relevant financial relationships.

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