

Radiation Plus Combination Immunotherapy May Help Preserve Bladder

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Patients with localized muscle-invasive bladder cancer (MIBC) who received radiation plus the immune checkpoint inhibitors (ICIs) durvalumab (Imfinzi) and tremelimumab (Imjudo) had durable responses that allowed for bladder preservation, according to results from the [IMMUNOPRESERVE](#) clinical trial published in [Clinical Cancer Research](#), a journal of the American Association for Cancer Research (AACR).

The standard of care for localized MIBC is radical cystectomy, the removal of the entire bladder. While it is typically effective, it can have lasting impacts on a patient's life, explained Xavier Garcia-del-Muro, MD, PhD, a professor of medical oncology at the University of Barcelona and the Institut Català d'Oncologia in Spain and senior author of the study.

"Radical cystectomy is a highly invasive surgery that can significantly impact patients' quality of life," Garcia-del-Muro said, citing self-consciousness and discomfort from urostomy bags and complications from reconstructed neobladders, among other issues. "Multimodal treatments offer a promising conservative alternative that deserves further exploration."

One noninvasive method under investigation involves transurethral resection of the tumor, followed by chemotherapy and radiation. While this approach has shown [promising results](#), chemotherapy is associated with significant toxicity, and up to half of patients may be ineligible, Garcia-del-Muro said.

By contrast, preclinical studies have [suggested](#) that a combination of ICIs that target different immune checkpoints—durvalumab, which targets PD-L1, and tremelimumab, which targets CTLA-4—may pair effectively with radiotherapy with fewer toxicities than chemotherapy. Further, radiotherapy can trigger cancer cells to release danger signals and other cytokines that can stimulate the immune system, potentially making ICIs more effective, Garcia-del-Muro explained.

He and his colleagues launched IMMUNOPRESERVE, a Phase II, multicenter, single-arm, open-label

clinical trial to assess the efficacy of radiation plus durvalumab and tremelimumab in patients with localized MIBC, with the goal of preserving patients' bladders. They enrolled and treated 32 patients with stage T2-T4a disease with no metastases or lymph node involvement who had not previously received immunotherapy (other than Bacillus Calmette-Guérin [BCG]) or radiotherapy to the bladder. Patients were either ineligible for or refused cystectomy. Enrolled patients were given three courses of durvalumab plus tremelimumab, each four weeks apart, with concurrent radiotherapy.

Among the 28 evaluable patients, 26 (93%) had a complete response. In the overall population, after two years of follow-up, five patients (16%) had experienced a metastatic recurrence, six patients (19%) had experienced a recurrence of muscle-invasive disease, and one patient (3%) had experienced a recurrence of non-muscle invasive disease.

After a median follow-up of 27 months, 30 patients were able to preserve their bladders, while two patients underwent radical cystectomy due to recurrence.

The estimated two-year overall survival and distant metastasis-free survival rates were 84% and 83%, respectively.

In terms of safety, Garcia-del-Muro considered the regimen well-tolerated. The incidence of grade 3 or 4 adverse events was 31%, and there was one treatment-related death. Eight patients (25%) did not receive the third planned dose of immunotherapy due to treatment-related toxicity.

"This multimodal bladder-preserving approach is feasible, showing high efficacy in terms of response and long-term bladder preservation," Garcia-del-Muro said. He and his colleagues aim to confirm these findings in larger studies with more patients, a longer follow-up, and direct comparisons to other treatment regimens including radiation plus chemotherapy.

"While this is an early exploratory study, the results are encouraging and highlight the potential of radiotherapy plus combination immunotherapy to improve quality of life without compromising survival," Garcia-del-Muro concluded.

Limitations of this study include a small sample size, relatively short follow-up period, and lack of comparison with other standard-of-care treatment options.

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