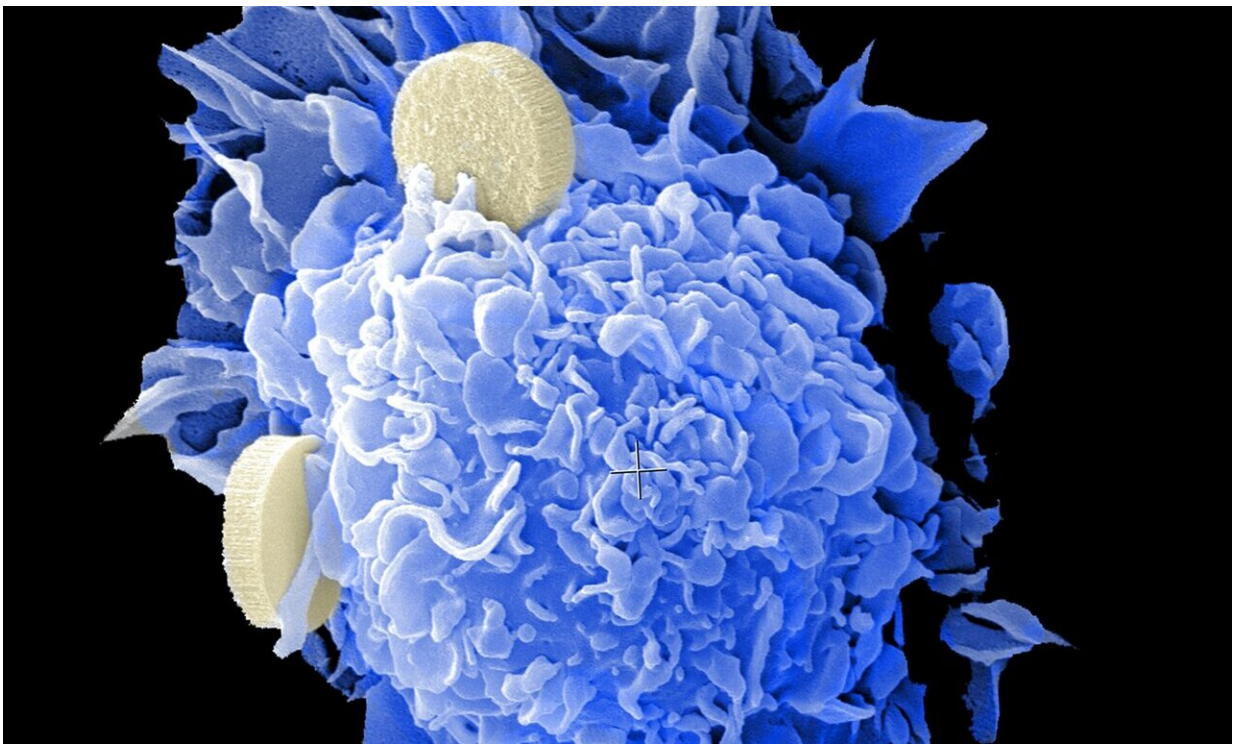
New combination therapy shows promise for bladder cancer patients unresponsive to standard treatment

June 6 2024



Credit: Unsplash/CC0 Public Domain

In an advance that could transform bladder cancer treatment, a novel combination of cretostimogene grenadenorepvec and pembrolizumab has shown remarkable efficacy in patients with Bacillus Calmette-Guérin

(BCG)-unresponsive non-muscle invasive bladder cancer.

Results from the phase 2 CORE-001 trial, published today in *Nature Medicine*, reveal a significant improvement in complete response rates and long-term disease control, offering new hope for patients with this challenging condition who face limited treatment options.

The trial included patients with BCG-unresponsive carcinoma in situ of the bladder, a condition that is notoriously difficult to treat and often leads to radical cystectomy. The combination therapy of intravesical cretostimogene grenadenorepvec (an intravesically delivered oncolytic immunotherapy) with systemic pembrolizumab (an immune checkpoint inhibitor) demonstrated a complete response rate of 57.1% at 12 months, surpassing previous benchmarks set by other therapies.

The trial also demonstrated durable responses; findings show a complete response rate of 82.9% at three months, with a median duration of response not yet reached after a median follow-up of 26.5 months.

"This study marks an important step forward in the treatment of BCG-unresponsive NMIBC," said Roger Li, M.D., principal investigator of the trial and urologic oncologist at Moffitt Cancer Center. "Our findings indicate that the combination of cretostimogene grenadenorepvec and pembrolizumab offers a unique, efficacious and durable bladder-preserving alternative strategy to radical cystectomy."

The oncolytic immunotherapy directly enters the bladder cancer cells, destroys them, and then stimulates an anti-tumor response from the body's immune system. Pembrolizumab, a well-known PD-1 inhibitor, further enhances the immune system's ability to attack cancer cells. The observed clinical benefits stem from the synergistic effect of these two therapies.

"These encouraging results highlight the potential for oncolytic immunotherapy to synergize with immune checkpoint inhibitors, offering a new avenue for patients who have exhausted other treatment options," Li said.

"We are optimistic that additional clinical trials will confirm these benefits and support the integration of both monotherapy and combination therapies into the standard-of-care for BCG-unresponsive non-muscle invasive bladder cancer."

The study noted that adverse events were manageable and consistent with those observed in previous monotherapy trials. The most common side effects related to cretostimogene were bladder-related symptoms, while pembrolizumab-related adverse events were typical of systemic immunotherapy.

The trial underscores the importance of innovative therapeutic approaches in oncology. Future research will focus on validating these findings in larger cohorts and exploring the underlying mechanisms of action.

More information: Oncolytic adenoviral therapy plus pembrolizumab in BCG-unresponsive non-muscle-invasive bladder cancer: the phase 2 CORE-001 trial., *Nature Medicine* (2024). DOI: 10.1038/s41591-024-03025-3

Provided by H. Lee Moffitt Cancer Center & Research Institute