Targeted therapy erdafitinib effective for patients with advanced bladder cancer and specific gene mutations

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Arlene Siefker Radtke M.D. Credit: MD Anderson Cancer Center

Treatment with the FGFR inhibitor erdafitinib in patients with metastatic bladder cancers marked by mutations in the FGFR3 gene resulted in a 40% overall response rate (ORR) and was well-tolerated, according to an international Phase II trial led by The University of Texas MD Anderson Cancer Center.

The trial results, published today in the *New England Journal of Medicine*, led to approval of erdafitinib in April by the Food and Drug Administration (FDA), making it the first targeted therapy approved for treating patients with advanced bladder cancer.

The oral targeted therapy also achieved a 59% ORR in patients for whom immunotherapy had previously failed, indicating this may be a viable option for these patients in need of alternative treatments. The findings were first reported at the 2018 American Society of Clinical Oncology Annual Meeting by principal investigator Arlene Siefker-Radtke, M.D., professor of Genitourinary Medical Oncology.

"Patients have been in desperate need for alternative strategies, especially when a large number of patients cannot tolerate the current standards of care," said Siefker-Radtke. "We were very gratified to see a 40% response rate in patients treated on this clinical trial. Not only did it work well in patients with lymph node metastases, but also in patients with high volume and very aggressive disease."

Standard of care for these cancers is cisplatin-based chemotherapy, an aggressive regimen with significant side effects, and this has largely

remained unchanged for several decades, explained Siefker-Radtke. Recently, immune checkpoint inhibitors have been approved for the treatment of advanced bladder cancer, but only 15 to 20% of patients see any benefit from these therapies, she said.

"I noticed that I wasn't seeing a great response to immune checkpoint inhibitors in my patients with FGFR3 mutations, which led me to wonder whether this would reflect a group of patients with an unmet need," said Siefker-Radtke. "When we heard about novel agents targeting this pathway, I became quite interested in exploring them in our bladder cancer patients."

Mutations in FGFR3 are present in approximately 15 to 20% of patients with metastatic bladder cancer and up to 35% of patients with other urothelial cancers, such as those of the renal pelvis and ureter. The international trial enrolled 99 patients with metastatic or surgically unresectable urothelial cancer and verified alterations in the FGFR3 gene.

Three patients in the trial had complete responses, or tumor disappearance, and 39 had percent stable disease. Median PFS was 5.5 months and median OS was 13.8 months. Among 22 patients previously treated with immunotherapy, 59% (13) had a partial or complete response.

"With a response rate of over 50% in patients previously treated with immunotherapy, the data suggest treatment with erdafitinib may be preferential for patients with FGFR3 mutations. However, this is preliminary evidence, so we need additional data to confirm this finding," said Siefker-Radtke.

All patients on the trial reported side effects from the therapy, with 21% discontinuing treatment due to adverse events and 67% reporting grade 3

or 4 adverse events. The most common treatment-related side effects were stomatitis (9%), nail dystrophy (6%), and hand-foot syndrome (5%).

Based on the results of the trial, the FDA granted a breakthrough therapy designation to erdafitinib in 2018 and approved the drug in April 2019 for treating patients with locally advanced or metastatic urothelial cancers with mutations in the FGFR2 or FGFR3 genes.

"With the recent approval of erdafitinib for the treatment of patients with FGFR3-mutant urothelial cancers, we now have an additional agent to add to our armamentarium," said Siefker-Radtke. "My hope is we will be able to add this to our treatment strategy, learn how it combines with immunotherapy and how we can use the effects of this drug to improve the survival for all of our bladder cancer patients."

A Phase III trial currently is underway to evaluate the efficacy of erdafitinib relative to chemotherapy or the checkpoint blockade inhibitor pembrolizumab in patients with metastatic urothelial cancer and FGFR3 mutations.

Provided by University of Texas M. D. Anderson Cancer Center