# Erdafitinib demonstrates improved responses in FGFR-altered advanced urinary tract cancers

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Targeted treatment with the fibroblast growth factor receptor (FGFR) inhibitor erdafitinib improved responses and overall survival compared to standard chemotherapy for patients with metastatic urothelial cancers with FGFR alterations. Results from the Phase III THOR trial, led by researchers at The University of Texas MD Anderson Cancer Center, were reported at the 2023 European Society of Medical Oncology (ESMO) Congress.

"Metastatic urothelial cancer continues to challenge us with its absence of a cure, highlighting the need for innovative treatment approaches," said Arlene Siefker-Radtke, M.D., professor of Genitourinary Medical Oncology and senior investigator on the trial. "This ongoing study presents compelling evidence that erdafitinib could potentially serve as a valuable targeted treatment option for individuals with FGFR alterations."

Genetic changes in FGFR are present in approximately 20% of patients with metastatic bladder cancer and up to 35% of patients with other urothelial cancers, including renal pelvis and ureter cancers. In 2019, erdafitinib was approved by the Food and Drug Administration for advanced FGFR-altered urothelial cancer based on the results of a Phase II trial led by Siefker-Radtke. It was the first approved FGFR-targeted therapy and is the only approved FGFR-targeted option for advanced urothelial cancer.

The ongoing randomized THOR trial, conducted at 121 sites in 23 countries, evaluated the efficacy and safety of erdafitinib in patients

with metastatic urothelial carcinoma and selected FGFR gene alterations. Patients were screened for the presence of FGFR gene alterations and assigned to two cohorts based on prior treatment with platinum-containing chemotherapy or immune checkpoint inhibitors.

## Erdafitinib significantly improved overall survival relative to chemotherapy in patients with prior immunotherapy

In the study's first cohort, published in the *New England Journal of Medicine*, 266 patients who had prior treatment with immune checkpoint inhibitors were randomized to receive either erdafitinib or chemotherapy.

The median overall survival (OS) was 12.1 months and 7.8 months, respectively, corresponding to a 36% lower risk of death for those treated with erdafitinib. The OS benefit was seen across subgroups, including age, type of FGFR alteration, number of prior lines of treatment, visceral metastasis, location of the primary tumor and type of chemotherapy.

Further, erdafitinib achieved a median progression-free survival of six months compared to just three months for chemotherapy. Nearly half (46%) of patients treated with erdafitinib had an objective response, meaning their tumors shrank, while just 12% on the chemotherapy arm had an objective response. The data from this cohort was first presented at the 2023 American Society of Clinical Oncology (ASCO) Annual Meeting.

## Erdafitinib achieves similar outcomes compared to pembrolizumab in immunotherapy-naïve patients

In the second cohort, published in the *Annals of Oncology*, 351 patients who had not received prior immunotherapy were randomized to receive either erdafitinib or pembrolizumab (anti-PD-1). There was no statistically significant difference in OS between the treatment arms, as erdafitinib had similar survival compared to immunotherapy in patients who received prior pembrolizumab.

Erdafitinib did achieve a median progression-free survival of 4.4 months compared to 2.7 months for pembrolizumab. Further, 40% of patients treated with erdafitinib had an objective response, while just 21.6% on the pembrolizumab arm had an objective response. There was a shorter duration of response with erdafitinib (4.3 months) than with pembrolizumab (24.4 months).

"The data from this new cohort provides early evidence suggesting there may be important impacts from the sequence of treatments for an FGFR3-altered urothelial cancer," Siefker-Radtke said. "Even though most primary FGFR-altered urothelial tumors are immunologically cold, it is possible that metastatic tumors may not share the same features. Perhaps these patients could benefit from combining erdafitinib with an immune checkpoint inhibitor."

Treatment-related adverse events across both cohorts were manageable and consistent with the known safety profile of erdafitinib. The impact of erdafitinib on the OS of patients with metastatic urothelial carcinoma and FGFR alterations highlights the importance of conducting molecular tests to identify FGFR alterations in individuals with metastatic urothelial cancer.

Further work is necessary to understand the impact of combining and sequencing erdafitinib with a checkpoint inhibitor. There may be a role for erdafitinib in patients with visceral crisis where rapid response and symptom improvement is indicated, thanks to its higher response rate.

**More information:** Yohann Loriot et al, Erdafitinib or Chemotherapy in Advanced or Metastatic Urothelial Carcinoma, *New England Journal of Medicine* (2023). DOI: 10.1056/NEJMoa2308849

A.O. Siefker-Radtke et al, Erdafitinib versus pembrolizumab in pretreated patients with advanced or metastatic urothelial cancer with select FGFR alterations: cohort 2 of the randomized phase III THOR trial, *Annals of Oncology* (2023). DOI: 10.1016/j.annonc.2023.10.003

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