Targeted therapy achieves responses across multiple cancer types with FGFR alterations

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Tumor type	ORR n/N (%)		
Total	64/217 (29.5)	Esophageal	1/8 (12.5)
Cholangiocarcinoma	16/31 (51.6)	Ovarian	2/8 (25.0)
High-grade glioma	3/30 (10.0)	Unknown primary	2/8 (25.0)
Pancreatic	10/18 (55.6)	Low-grade glioma	2/7 (28.6)
Breast	5/16 (31.3)	Salivary gland	5/5 (100.0)
Squamous NSCLC	3/14 (21.4)	Duodenal	1/1 (100.0)
Nonsquamous NSCLC	3/9 (33.3)	Thyroid	1/1 (100.0)
Endometrial	4/8 (50.0)		

Primary analysis results from RAGNAR, the largest tumor agnostic trial of targeted tx to date, confirm efficacy of erda in heavily pretreated pts with FGFRalt advanced solid tumors. Erda activity was observed in adults and adolescents across tumor types, and across FGFR1-3 gene mutations and fusions. Erda tolerability was consistent with its known safety profile. Clinical trial information: NCT04083976. Credit: University of Texas M. D. Anderson Cancer Center

Three clinical trials led by researchers at The University of Texas MD Anderson Cancer Center demonstrated positive results from the targeted

therapy erdafitinib for patients with multiple tumor types harboring FGFR alterations. The data are being presented at the 2023 American Society of Clinical Oncology (ASCO) Annual Meeting.

Erdafitinib is an oral medication that blocks the activity of FGFR signaling proteins, which are important for a variety of normal cellular processes. However, FGFR genetic alterations can drive the development of many cancer types, including urothelial, bile duct, breast, stomach, liver and lung cancers. Erdafitinib was the first approved FGFR-targeted therapy and is the only approved FGFR-targeted option for advanced urothelial cancer.

Erdafitinib demonstrates tumor-agnostic benefits across 16 cancer types

The tumor-agnostic Phase II RAGNAR trial, led by Shubham Pant, M.D., professor of Gastrointestinal Medical Oncology and Investigational Cancer Therapeutics, confirmed the efficacy of erdafitinib in heavily pre-treated patients with advanced FGFR-altered solid tumors across 16 distinct cancer types.

Among 217 patients on the trial, the overall response rate (ORR) was 29.5%, including six complete responses and 58 partial responses. The ORR was comparable across FGFR1-3 mutations and fusions. The treatment achieved a disease control rate of 73.7% and a clinical benefit rate of 45.6%, including an ORR of 56% in patients with pancreatic cancer and 52% in cholangiocarcinoma.

"This study represents the largest tumor-agnostic trial of a targeted therapy to date, and the results demonstrate that erdafitinib provides meaningful clinical benefit in patients with advanced FGFR-altered solid tumors," Pant said. "These findings suggest erdafitinib may be an

important option, regardless of tumor type, for patients with FGFR alternations who have exhausted other available therapies."

The ongoing open-label, single-arm trial enrolled adult and pediatric patients with FGFR-altered advanced solid tumors, excluding urothelial cancers. All patients had disease progression after at least one prior systemic therapy and had no alternative treatment options.

The median age of participants was 57 years, with a range of 12-79 years, and patients had received a median of two prior lines of therapy. The study included patients with central nervous system tumors, gastrointestinal cancers, gynecologic cancers, lung cancers and other rare tumors.

All but one patient experienced treatment-emergent side effects, and 70% of participants experienced grade 3 or higher adverse events. The safety profile was consistent with the known side effects seen in previous trials.

The trial was supported by Janssen Research & Development, LLC. A complete list of collaborating authors and disclosures can be found with the abstract here.

Adding immunotherapy to erdafitinib elevates response rates in advanced urinary tract cancers

The Phase II NORSE study, led by Arlene Siefker-Radtke, M.D., professor of Genitourinary Medical Oncology, demonstrated clinically meaningful improvements when adding the immunotherapy cetrelimab to erdafitinib for patients with FGFR-altered metastatic urothelial, or urinary tract, cancers.

The combination of erdafitinib with cetrelimab, an anti-PD-1 immune checkpoint inhibitor, achieved an ORR of 54.5% across 44 patients, with six complete responses (CRs) and an overall survival (OS) rate of 68% at 12 months. In comparison, erdafitinib alone achieved an ORR of 44.2% in 43 patients, including one CR and a 12-month OS rate of 56%.

"FGFR-altered tumors typically are immunologically cold and have limited responses to immunotherapy. The goal of this trial was to determine if combining immunotherapy and FGFR-targeted therapy could improve response rates," Siefker-Radtke said. "We are encouraged by the promising responses and median survival results, and we look forward to future studies to learn the full impact for our patients."

Standard therapy for patients with advanced urothelial cancer is cisplatin-based chemotherapy, but this regimen has significant side effects and cannot be tolerated by all patients. This open-label study was designed to evaluate the safety and efficacy of erdafitinib plus cetrelimab versus erdafitinib alone in adult patients who had received prior systemic therapy and were ineligible for cisplatin-based therapies.

As of the data cutoff, the trial randomized 87 patients across the treatment arms. Median ages were 69 and 72 on the combination and monotherapy arms, respectively. The median follow-up time was 14.2 months.

The combination presented a safety profile consistent with that of erdafitinib and cetrelimab alone. Grade 3 treatment-related adverse events occurred in 45.5% of patients receiving the combination treatment and 46.5% of patients receiving erdafitinib alone. There was one cetrelimab-related patient death in the combination arm that occurred secondary to pulmonary failure.

The trial was supported by Janssen Research & Development, LLC. A

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Erdafitinib significantly improves patient outcomes over chemotherapy in FGFR-altered urinary tract cancers

According to results from cohort one of the Phase III THOR trial, erdafitinib significantly improved survival and response outcomes relative to standard chemotherapy for patients with advanced or metastatic urothelial cancers with FGFR alterations.

With 266 patients randomized to receive either erdafitinib or chemotherapy, the median OS was 12.1 and 7.8 months, respectively, corresponding to a 36% lower risk of death for those treated with erdafitinib. Further, erdafitinib achieved a median progression-free survival of 5.6 months compared to just 2.7 months for chemotherapy. Nearly half (46%) of patients treated with erdafitinib saw their tumors shrink, while just 12% on the chemotherapy arm had an objective response.

"These results demonstrate improved responses and survival outcomes for patients receiving erdafitinib compared to standard-of-care chemotherapy, confirming the benefit for these patients," said Siefker-Radtke, senior investigator on the trial. "This highlights the significance of a targeted therapy option for patients with FGFR-altered urothelial cancer and is the first biomarker-targeted therapy for this disease."

Erdafitinib was approved in 2019 by the Food and Drug Administration for advanced FGFR-altered urothelial cancer based on results of a Phase II trial led by Siefker-Radtke. The current trial reinforces the benefits over standard therapeutic options for these patients.

The trial enrolled adults with advanced/metastatic urothelial cancer harboring specific FGFR alterations. All patients had experienced progression after two or fewer prior lines of therapy, including chemotherapy and immunotherapy. Patients were randomized to receive erdafitinib (136) or the investigator's choice of chemotherapy (130). The patients' median age was 67.

Cohort one of the trial met its primary endpoint of improved OS and was concluded based on achieving predefined superiority criteria. The side effects of the treatment were consistent with the known safety profile of erdafitinib.

More information: Conference: conferences.asco.org/am/attend

Abstract: meetings.asco.org/abstracts-presentations/220271

Abstract: meetings.asco.org/abstracts-presentations/218071

Abstract: meetings.asco.org/abstracts-presentations/226592

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