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Erdafitinib in patients with advanced solid tumours with FGFR alterations (RAGNAR): an international, single-arm, phase 2 study

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Abstract

Background: FGFR alterations are reported across various malignancies and might act as oncogenic drivers in multiple histologies. Erdafitinib is an oral, selective pan-FGFR tyrosine kinase inhibitor with activity in FGFR-altered advanced urothelial carcinoma. We aimed to evaluate the safety and activity of erdafitinib in previously treated patients with FGFR-altered advanced solid tumours.

Methods: The single-arm, phase 2 RAGNAR study was conducted at 156 investigative centres (hospitals or oncology practices that are qualified oncology study centres) across 15 countries. The study consisted of four cohorts based on tumour histology and patient age; the results reported in this Article are for the primary cohort of the study, defined as the Broad Panel Cohort, which was histology-agnostic. We recruited patients aged 12 years or older with advanced or metastatic tumours of any histology (except urothelial cancer) with predefined FGFR1-4 alterations (mutations or fusions according to local or central testing). Eligible patients had disease progression on at least one previous line of systemic therapy and no alternative standard therapy available to them, and an Eastern Cooperative Oncology Group performance status of 0-1 (or equivalent for adolescents aged 12-17 years). Patients received once-daily oral erdafitinib (8 mg/day with provision for pharmacodynamically guided up-titration to 9 mg/day) on a continuous 21-day cycle until disease progression or intolerable toxicity. The primary endpoint was objective response rate by independent review committee according to Response Evaluation Criteria In Solid Tumors (RECIST), version 1.1, or Response Assessment In Neuro-Oncology (RANO). The primary analysis was conducted on the treated population of the Broad Panel Cohort. This ongoing study is registered with ClinicalTrials.gov, number NCT04083976.

Findings: Patients were recruited between Dec 5, 2019, and Feb 15, 2022. Of 217 patients treated with erdafitinib, 97 (45%) patients were female and 120 (55%) were male. The data cutoff was Aug 15, 2022. At a median follow-up of 17·9 months (IQR 13·6-23·9), an objective response was observed in 64 (30% [95% CI 24-36]) of 217 patients across 16 distinct tumour types. The most common grade 3 or higher treatment-emergent adverse events related to erdafitinib were stomatitis (25 [12%]),

palmar-plantar erythrodysaesthesia syndrome (12 [6%]), and hyperphosphataemia (11 [5%]). The most commonly occurring serious treatment-related adverse events (grade 3 or higher) were stomatitis in four (2%) patients and diarrhoea in two (1%). There were no treatment-related deaths.

Interpretation: RAGNAR results show clinical benefit for erdafitinib in the tumour-agnostic setting in patients with advanced solid tumours with susceptible FGFR alterations who have exhausted other treatment options. These results support the continued development of FGFR inhibitors in patients with advanced solid tumours.

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