

Erdaftinib for advanced urothelial carcinoma

Treatment with erdaftinib, a tyrosine kinase inhibitor of FGFR1–4, had antitumour activity in patients with advanced urothelial carcinoma with mutations in fibroblast growth factor receptor (FGFR), according to a new study by Johann Loriot and colleagues.

99 patients with locally advanced and unresectable or metastatic urothelial carcinoma, and at least one *FGFR3* mutation or fusion of *FGFR2* and *FGFR3*, were included in the phase 2 trial. Patients were assigned to receive a continuous regimen of 8 mg per day of erdaftinib, with the possibility of an increase to 9 mg per day. The primary endpoint was the proportion of patients achieving an objective response. Secondary endpoints included progression-free survival, overall survival, and response according to subgroups.

After a median of 5 monthly cycles of erdaftinib (range 1–18), 40 (40%) of

99 patients had an objective response. Median progression-free survival was 5.5 months (95% CI 4.2–6.0) and median overall survival was 13.8 months (95% CI 9.8 to not reached). The response to erdaftinib was not affected by the type or the number of previous therapies, or by the presence of visceral metastases. 13 (59%) of 22 patients who had previously received immunotherapy had an objective response to erdaftinib. Treatment-related adverse events of grade 3 or worse were reported in 46% of patients and were mostly managed with dose adjustments.

“This is a patient population who have a poor prognosis”, said coauthor Arlene Siefker-Radtke (University of Texas MD Anderson Cancer Center, Houston, TX, USA). “With immunotherapy, one of the limitations has been the lower response rate seen in patients with visceral metastases, but that was not the case in our

study.” Mark Linch (University College London Cancer Institute, London, UK) welcomed the findings. “For the first time in this disease, we can see that patients with particular mutations have a higher chance of responding to a targeted therapy”, he said. “It also seems that we have a subgroup of patients who may be less likely to benefit from immunotherapy and more likely to benefit from erdaftinib.”

Siefker-Radtke is principal investigator for an ongoing phase 3 trial comparing erdaftinib with docetaxel or pembrolizumab in patients with advanced urothelial cancer and *FGFR* gene alterations. “Bladder cancer is composed of a variety of cancers that differ in their mutation pattern and in their gene expression; that may help us predict which therapy is best for a specific patient”, she added.

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For the study by Loriot and colleagues see *N Engl J Med* 2019; **381**: 338–48