Derazantinib for intrahepatic cholangiocarcinoma

Derazantinib—an orally bioavailable, multikinase inhibitor with potent pan-fibroblast growth factor receptor (FGFR) activity—has preliminary anti-tumour activity and a manageable safety profile in patients with unresectable or metastatic FGFR2 fusion-positive intrahepatic cholangiocarcinoma, according to a recent study.

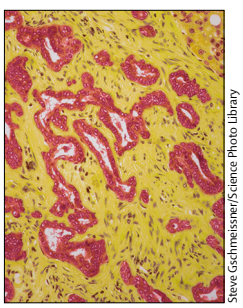
In the multicentre, open-label, phase 1–2 trial, Vincenzo Mazzaferro (Istituto Nazionale Tumori IRCCS, Milan, Italy) and colleagues enrolled 29 patients with unresectable intrahepatic cholangiocarcinoma with FGFR2 fusion. All patients had either progressed after at least one previous systemic therapy (n=27) or were treatment-naive but not eligible for first-line chemotherapy (n=2). Derazantinib was given in 28-day, continuous, uninterrupted treatment cycles. Two patients received derazantinib 400 mg daily as part of the phase 1 trial, whereas 27 patients received derazantinib 300 mg daily (the recommended phase 2 dose). Tumour response was assessed every 8 weeks. The primary endpoint was safety and tolerability.

At a median follow-up of 6·7 months (range 2·9–19·4), six (21%) of 29 patients had achieved a partial response, with a median duration of response of 4·6 months (95% CI 2·3–8·9). 24 (83%) patients achieved disease control (a partial response or stable disease), with a median duration of disease control of 5·8 months (95% CI 5·3–8·4 months). Median progression-free survival was 5·7 months (95% CI 4·0–9·2). At data cutoff, 27 (93%) patients had discontinued treatment, mostly because of confirmed disease progression (n=15 [52%]), adverse events (n=4 [14%]), or clinical deterioration (n=4 [14%]). Any-grade treatment-related adverse events occurred in 27 (93%) patients, although only eight (28%) patients had grade 3 or worse adverse events.

"This trial highlights the importance of identifying patients with intrahepatic cholangiocarcinoma and FGFR2 translocation for treatment with selective FGFR inhibitors such as derazantinib," explained co-author Bassel El-Rayes (Emory University, Atlanta, GA, USA).

"Chemotherapeutic [options] for intrahepatic cholangiocarcinoma are currently very limited, and [it] is still a dismal disease", stated Junji Furuse (Kyorin University, Tokyo, Japan). "Although there are not many patients with FGFR2 gene fusion, it would be of value to develop FGFR inhibitors for advanced intrahepatic cholangiocarcinoma to improve survival."

Elizabeth Gourd



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For the **study by Mazzaferro and colleagues** see *Br J Cancer* 2018; published online Nov 13. DOI:10.1038/s41416-018-0334-0