BGJ398 for *FGFR*-altered advanced cholangiocarcinoma

Results from a single-arm, multicentre, phase 2 trial suggest that patients with advanced cholangiocarcinoma with genetic alterations in fibroblast growth factor receptor *(FGFR)* might respond to treatment with BGJ398, a first-in-class selective pan-FGFR kinase inhibitor.

In the study, Milind Javle (MD Anderson Cancer Center, Houston, TX, USA) and colleagues enrolled 61 patients with metastatic or advanced *FGFR*-altered cholangiocarcinoma who did not respond to first-line gemcitabine-based chemotherapy. Patients received oral BGJ398 (125 mg) once daily in 4-week cycles (3 weeks on drug, 1 week off).

The primary endpoint of investigator-assessed overall response to BGJ398 was achieved by nine patients (14·8%; 95% CI 7·0–26·2); all were partial responses. 46 patients (75·4%; 62·7–85·5) achieved disease control (partial response or stable disease). Median progression-free survival was 5·8 months (95% CI 4·3–7·6). The most common treatment-related adverse events were hyperphosphataemia (in 44 [72%] patients), fatigue (22 [36%]), stomatitis (18 [30%]), and alopecia (16 [26%]). Grade 3–4 treatment-related adverse events occurred in 25 (41%) patients, including hyperphosphataemia (ten [16%]), stomatitis (four [7%]), and palmar-plantar erythrodysesthesia (3 [5%]). Toxicity was generally manageable. Some mitigation of dosing to manage toxicities was needed by many patients to remain on treatment.

Javle commented that there is no standard treatment for advanced cholangiocarcinoma in the second-line setting. He summarised the study, saying "mutational profiling of cholangiocarcinoma has clinical utility, and *FGFR2* fusions can be targeted by FGFR-specific drugs like BGJ398. There's a subset of cholangiocarcinoma patients who are better served with targeted therapy rather than chemotherapy, and the role of these targeted agents in first- and second-line needs further investigation."

Daniel Catenacci (University of Chicago Medical Center, Chicago, IL, USA) noted that patients in this study were mostly heavily pretreated; 20% had four or more previous lines of therapy. "Nothing was working for these patients, and a median progression-free survival of 5·8 months is on par with first-line chemotherapy." Catenacci added that a number of competitor drugs are being tested in trials for this subgroup of cholangiocarcinomas, and that he commends the investigators: "this study will really move the field forward."

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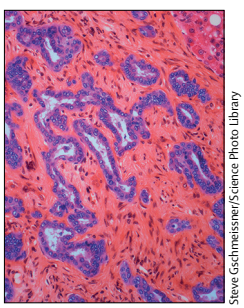

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For the **study by Javle and colleagues** see *J Clin Oncol* 2017; published online Nov 28. DOI:10.1200/JCO.2017.75.5009