

832TiP Infigratinib versus gemcitabine plus cisplatin multicenter, open-label, randomized, phase III study in patients with advanced cholangiocarcinoma with FGFR2 gene fusions/translocations: The PROOF trial

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Background: Cholangiocarcinoma is the most common biliary tract malignancy with an estimated incidence in Europe of 0.4–1.8/100,000 patients, and approximately 5,000–10,000 new cases annually in the USA. Treatment options are limited with a need to provide increased disease control, improved outcome, and targeted therapy that is less toxic than standard chemotherapy. The fibroblast growth factor receptor (FGFR) family plays an important role in cholangiocarcinoma, with FGFR2 gene fusions detected in about 15% of patients. Infigratinib is an ATP-competitive, FGFR1–3-selective oral tyrosine kinase inhibitor. Based on preliminary evidence of infigratinib efficacy in patients with relapsed/refractory cholangiocarcinoma with FGFR2 fusions/translocations (phase 2 study CBJG398X2204), the PROOF trial is evaluating infigratinib versus gemcitabine + cisplatin in front-line patients with advanced cholangiocarcinoma with FGFR2 gene fusions/translocations.

Trial design: Patients with advanced/metastatic or inoperable cholangiocarcinoma are randomized 1:1 to oral infigratinib once daily for 21 days of a 28-day treatment cycle versus intravenous gemcitabine (1000 mg/m²) plus cisplatin (25 mg/m²) on days 1&8 of a 21-day cycle. Treatment will continue until confirmed progressive disease by central review, intolerance, withdrawal of informed consent, or death. After 8 cycles of gemcitabine plus cisplatin, patients can continue treatment if the investigator considers that they are deriving continued benefit. Patients on the gemcitabine plus cisplatin arm who progress can cross-over to infigratinib. The primary endpoint is progression-free survival (PFS, RECIST v1.1 central review). Secondary endpoints include overall survival, PFS (investigator determined), overall response rate, disease control rate, duration of response, and safety. Quality of life, PK and exploratory genetic alterations/biomarkers will also be measured. The study was initiated in February 2019 with planned enrollment of 350 patients with confirmed FGFR2 gene fusions/translocations.

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