SO-4 Progression-free survival in patients with cholangiocarcinoma with FGFR2 fusions or rearrangements: A FIGHT-202 post-hoc analysis of prior systemic therapy response

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Background: Most cholangiocarcinoma (CCA) patients are diagnosed with advanced disease and are ineligible for surgery. First-line, standard-of-care therapy for patients with advanced/metastatic CCA not amenable to surgery is gemcitabine plus cisplatin. FGFR2 fusions or rearrangements are oncogenic drivers of CCA and are almost exclusive to intrahepatic CCA (iCCA; prevalence, 10–15%). However, the role of this alteration and how it impacts patient response to systemic therapy remains uncharacterized. FIGHT-202 is a phase 2 study of pemigatinib (a selective, potent, oral fibroblast growth factor receptor [FGFR]1–3 inhibitor) in patients with locally advanced or metastatic CCA with or without FGF/FGFR genomic alterations who progressed on ≥1 prior therapy (NCT02924376; Abou-Alfa et al. Lancet Oncol 2020;21:671–84). This post-hoc analysis evaluated progression free survival (PFS) to standard systemic therapy before FIGHT-202 study enrollment, in patients with CCA harboring FGFR2 fusions or rearrangements (FGFR2+).

Methods: In FIGHT-202, patients with locally advanced/metastatic CCA with documented disease progression following ≥1 previous systemic therapy were assigned to cohorts based on the presence and type of FGF/FGFR alterations. For this analysis, electronic case report forms from patients with FGFR2+ CCA enrolled in FIGHT-202 were reviewed to determine disease history and exposure to prior lines of systemic cancer therapies (LOSCT) in the advanced setting before receiving pemigatinib. Only patients with sufficient data on prior LOSCT were included in this analysis. Median PFS was calculated using the Kaplan-Meier method, defined as the date of initiation of that LOSCT until the date of progression.

Results: For the 108 patients with FGFR2+ CCA included in this analysis (April 2020 datacut), previous systemic therapy before pemigatinib most commonly included pyrimidine analogues (99.1%) or platinum compounds (96.3%), 99% had iCCA, median age was 55.5 years, and 61% were female. Median PFS on first-line therapy received prior to FIGHT-202 enrollment was 5.6 (95% confidence interval [CI]: 4.0, 8.3) months (n=104). Median PFS on second-line therapy received prior to FIGHT-202 enrollment was 4.4 (95% CI: 3.0, 5.3) months (n=40). For patients who had progressed after only 1 line of prior therapy and then received pemigatinib second-line during FIGHT-202, median PFS was 7.0 (95% CI: 4.9, 11.1) months (n=65). Median PFS on third-line therapy received prior to FIGHT-202 enrollment was 6.6 (95% CI: 2.7, 9.7) months (n=13). For patients who had progressed after 2 lines of prior therapies and then received pemigatinib third-line during FIGHT-202, median PFS was 8.9 (95% CI: 4.9, 13.1) months (n=30).

Conclusions: This post-hoc analysis provides data about PFS on standard systemic therapies received before pemigatinib for patients with FGFR2+ CCA. The short PFS on these standard therapies in patients with FGFR2+ CCA highlights the need for development of other options including targeted therapies to improve outcomes. Median PFS on second- or third-line pemigatinib for FGFR2+ CCA was longer than second- or third-line systemic therapy received prior to FIGHT-202 enrollment. Limitations of this analysis include retrospective examination of investigator reported data and small patient numbers for some analyses.

Clinical trial identification: NCT02924376.

Legal entity responsible for the study: Incyte Corporation.

Funding: Incyte Corporation.

Disclosure: G. Abou-Alfa: Advisory / Consultancy: Agios, Astra Zeneca, Alnylam, Autem, Bayer, Beigene, Berry Genomics, Celgene, CytomX, Eisai, Eli Lilly, Exelixis, Flatiron, Genentech/Roche, Genoscience, Helio, Incyte, Ipsen, Legend Biotech, Loxo, Merck, MINA, QED, Redhill, Rafael, Silenseed, Sillaj; Research grant / Funding (self): Arcus, Agios, Astra Zeneca, Bayer, BioNtech, BMS,

Celgene, Flatiron, Genentech/Roche, Genoscience, Incyte, Polaris, Puma, QED, Sillajen, Yiviva. G. Vaccaro: Advisory / Consultancy: Incyte, Pfizer, Merck, Taiho; Speaker Bureau / Expert testimony: Incyte. A. Paulson: Advisory / Consultancy: Incyte; Research grant / Funding (institution): Incyte. M. Borad: Research grant / Funding (institution): Celgene. E. Van Cutsem: Advisory / Consultancy: Array, Astellas, Astrazeneca, Bayer, Beigene, Biocartis, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Daiichi, Halozyme, GSK, Incyte, Ipsen, Lilly, Merck Sharp & Dohme, Merck KGaA, Novartis, Pierre Fabre, Roche, Servier, Sirtex, Taiho; Research grant / Funding (institution): Amgen, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Ipsen, Lilly, Merck Sharp & Dohme, Merck KGaA, Novartis, Roche, Servier. C. Lihou: Shareholder / Stockholder / Stock options: Incyte Corporation. H. Ren: Shareholder / Stockholder / Stock options: Incyte Corporation. K. Bibeau: Shareholder / Stockholder / Stock options: Incyte Corporation; Full / Part-time employment: Incyte Corporation. L. Feliz: Shareholder / Stockholder / Stock options: Incyte; Full / Part-time employment: Incyte. A. Vogel: Honoraria (self): Daiichi Sankyo, AstraZeneca; Advisory / Consultancy: Daiichi Sankyo, AstraZeneca. All other authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2021.05.028