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NCCN® Guidelines Panel: Hepatobiliary

On behalf of Incyte Corporation, I respectfully request the NCCN Hepatobiliary Guideline Panel review and consider the enclosed data for PEMAZYRE™ (pemigatinib) for the treatment of adults with previously treated, unresectable locally advanced or metastatic cholangiocarcinoma with a fibroblast growth factor receptor 2 (FGFR2) fusion or other rearrangement.

Specific Changes: We request inclusion of pemigatinib as a treatment option for adults with previously treated, unresectable locally advanced or metastatic cholangiocarcinoma with a fibroblast growth factor receptor 2 (FGFR2) fusion or other rearrangement. Also, in order to detect the broad range (>125)¹ of FGFR2 fusion partners and rearrangements, as well as other actionable genomic alterations observed in patients with cholangiocarcinoma, we request the panel recommend molecular testing using next generation sequencing (NGS) panels. The NGS panel should have the ability to detect unknown fusions and rearrangements, in addition to known fusions. We request the recommendation that molecular testing be carried out early, ideally at diagnosis, in order to facilitate treatment decision-making. In addition to determining eligibility for approved therapies, molecular testing may be used to screen for clinical trial participation. This guidance is consistent with recommendations made in the NCCN Bladder Cancer guidelines.

FDA Clearance: On April 17, 2020, the FDA approved PEMAZYRE, an FGFR 1, 2 and 3 inhibitor, for the treatment of adults with previously treated, unresectable locally advanced or metastatic cholangiocarcinoma with a fibroblast growth factor receptor 2 (FGFR2) fusion or other rearrangement as detected by an FDA-approved test.² This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s). Please refer to the enclosed prescribing information for the full FDA-approved indication and safety information.

Rationale: Fight-202 was a multicenter, open-label, single-arm, Phase II study to evaluate the efficacy and safety of pemigatinib in previously treated patients with unresectable locally advanced or metastatic cholangiocarcinoma.^{2,3} Eligibility criteria included documented FGF/FGFR status as determined by clinical trial assay (FoundationOne® CDx), progression after ≥1 prior therapy, and Eastern Cooperative Oncology Group Performance Status rating of ≤2.³ Patients were enrolled into 1 of 3 cohorts based on their FGF/FGFR status:

- Cohort A: FGFR2 fusions/rearrangements
- Cohort B: other FGF/FGFR genetic alterations
- Cohort C: no FGF/FGFR genetic alterations

The primary endpoint was confirmed overall response rate (ORR) in cohort A. Secondary endpoints included ORR in cohorts B, A+B, and C; duration of response, disease control rate, progression-free survival (PFS), overall survival, and safety in all cohorts. The study was not designed to make statistical comparisons between cohorts.

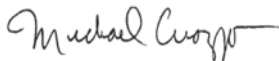
The ORR in cohort A (n=107) was 35.5% (95% confidence interval [CI], 26.5%-45.4%), including 2.8% complete response (CR) and 32.7% partial response (PR). The stable disease and disease control rates in cohort A were 46.7% and 82%, respectively.³ The median duration of response was 9.1 months (95% CI, 6-14.5 months).² Median OS and PFS in cohort A in were 21.1 months (95% CI, 14.8-NE) and 6.9 months (95% CI, 6.2-9.6), respectively.³ No responses were observed in cohort B (n=20) or C (n=18). The most common adverse events ($\geq 40\%$) in cohorts A-C (n=146) were hyperphosphatemia (60%), alopecia (49%), diarrhea (47%), fatigue (43%), nail toxicities (42%), nausea (40%), and dysgeusia (40%). Serous retinal detachments occurred in 4% of patients. The most common grade ≥ 3 adverse events ($\geq 5\%$) were hypophosphatemia (12%), arthralgia (6%), hyponatremia (6%), stomatitis (5%), abdominal pain (5%), and fatigue (5%).³

The following articles are submitted in support of this proposed change. We would like to acknowledge the contributions of NCCN panel members who are also co-authors or co-contributors of these publications.

1. Javle M, Murugesan K, Shroff R, et al. Profiling of 3,634 cholangiocarcinomas (CCA) to identify genomic alterations (GA), tumor mutational burden (TMB), and genomic loss of heterozygosity (gLOH). J Clin Oncol 2019;37:4087.
2. Pemazyre [[Prescribing Information](#)] Wilmington, DE: Incyte.
3. Abou-Alfa G, Sahai V, Hollebecque A, et al. Pemigatinib for previously treated, locally advanced or metastatic cholangiocarcinoma: a multicentre, open-label, phase 2 study. Lancet Oncol 2020; published online March 20. [https://doi.org/10.1016/S1470-2045\(20\)30109-1](https://doi.org/10.1016/S1470-2045(20)30109-1).

We appreciate the Panel's review and consideration of this submission. Should you have any questions or would like additional information, please do not hesitate to contact me.

Sincerely,



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