The Medical Letter®

on Drugs and Therapeutics

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Online Article

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IN BRIEF

A New Indication for Pemigatinib *(Pemazyre)*

The oral kinase inhibitor pemigatinib (*Pemazyre* – Incyte) has been approved by the FDA for treatment of adults with relapsed or refractory myeloid/lymphoid neoplasms (MLNs) with fibroblast growth factor receptor 1 (FGFR1) rearrangements. It is the first targeted therapy to be approved in the US for this indication. The drug received accelerated approval from the FDA in 2020 for treatment of adults with previously treated, unresectable, locally advanced or metastatic cholangiocarcinoma with FGFR2 fusions or other rearrangements.[1]

MECHANISM OF ACTION — Alterations in genes encoding FGFR can lead to proliferation, migration, and survival of malignant cells. Pemigatinib inhibits FGFR1, 2, and 3, blocking phosphorylation and signaling and causing cell death.

CLINICAL STUDIES — FDA approval of pemigatinib for the new indication was based on the results of an ongoing open-label trial (FIGHT-203) that included 28 patients with relapsed or refractory MLNs with FGFR1 rearrangements. Patients could have relapsed after allogeneic hematopoietic stem cell transplantation (allo-HSCT) or a disease-modifying therapy or were not candidates for allo-HSCT or other disease-modifying therapies. Patients received pemigatinib 13.5 mg once daily (2 weeks on, 1 week off or continuously) until disease progression or unacceptable toxicity occurred or until patients were able to receive an allo-HSCT. Of the 18 patients with chronic phase in the marrow with or without extramedullary disease (EMD), 14 patients (78%) achieved a complete response. The median time to a complete response was 104 days and the median duration of complete response was not reached. In the 4 patients with blast phase in the marrow with or without EMD, 2 patients achieved a complete response. In the 3 patients with EMD only, 1 achieved a complete response. For all 28 patients, the complete cytogenetic response rate was 79%. The trial is expected to be completed this year.[2]

ADVERSE EFFFECTS — The most common adverse effects of pemigatinib in the FIGHT-203 trial were hyperphosphatemia, diarrhea, stomatitis, and anemia. Decreased appetite, nail toxicity, alopecia, rash, dry skin, palmar-plantar erythrodysesthesia, GI adverse effects, dry eye, fatigue, and epistaxis can occur. The drug can also cause retinal pigment epithelial detachment; an ophthalmologic exam should be conducted before starting treatment, every 2 months for the first 6 months, and every 3 months thereafter.

DRUG INTERACTIONS — Pemigatinib is metabolized primarily by CYP3A4 *in vitro*. Concomitant use of a strong or moderate CYP3A4 inhibitor and pemigatinib is not recommended. The dose of pemigatinib should be reduced from 13.5 mg to 9 mg or from 9 mg to 4.5 mg if concurrent use of a CYP3A4 inhibitor is necessary. Concurrent use of pemigatinib and strong or moderate CYP3A4 inducers should be avoided.[3]

PREGNANCY AND LACTATION — Pemigatinib caused fetal malformations and embryofetal death in animal studies. Women of reproductive potential and their male partners should use effective contraception during treatment with pemigatinib and for 1 week after the last dose. There are no data on the presence of pemigatinib in human breast milk or its effects on the breastfed infant or milk production. Women should avoid breastfeeding during treatment with pemigatinib and for 1 week after the last dose.

DOSAGE, ADMINISTRATION, AND COST — The recommended dosage of pemigatinib for the new

indication is 13.5 mg once daily until disease progression or unacceptable toxicity occurs. The label includes dosage adjustments that should be made if adverse effects occur. The dose of pemigatinib should be reduced to 9 mg in patients with severe renal or hepatic impairment. A 30-day supply of *Pemazyre* costs $38,646.30.[4] ■

1. Pemigatinib (Pemazyre) for cholangiocarcinoma. Med Lett Drugs Ther 2020; 62:e208.
2. J Gotlib et al. A phase 2 study of pemigatinib (FIGHT-203; INCB054828) in patients with myeloid/lymphoma neoplasms (MLNs) with fibroblast growth factor receptor 1 (FGFR1) rearrangement (MLN^{FGFR1}). Blood 2021; 138(Suppl1):385.
3. Inhibitors and inducers of CYP enzymes, P-glycoprotein, and other transporters. Med Lett Drugs Ther 2023 January 25 (epub). Available at: medicalletter.org/downloads/CYP_PGP_Tables.pdf.
4. Approximate WAC. WAC = wholesaler acquisition cost or manufacturer's published price to wholesalers; WAC represents a published catalogue or list price and may not represent an actual transactional price. Source: AnalySource® Monthly. April 5, 2023. Reprinted with permission by First Databank, Inc. All rights reserved. ©2023. www.fdbhealth.com/policies/drug-pricing-policy.

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