NEW DRUGS

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Pemigatinib

Approved indication: cholangiocarcinoma

Pemazyre (Specialised Therapeutics)
4.5 mg, 9 mg and 13.5 mg tablets

Cancers of the bile duct (cholangiocarcinoma) are relatively rare. Surgery may not be possible and relapse rates are high. Even with combination chemotherapy, the prognosis is poor. In patients with metastatic disease, survival may be less than 12 months.

Genetic research has found that some patients have alterations in the genes for fibroblast growth factor receptors (FGFR). These receptors may induce the proliferation of cancer cells. As the receptors contain tyrosine kinases, a kinase inhibitor could have beneficial effects.

Pemigatinib is an inhibitor of FGFR1, 2 and 3. A dose of 13.5 mg is taken once daily for 14 days followed by a seven-day break. Food has little effect on absorption. Most of the dose is metabolised by cytochrome P450 (CYP) 3A4 and excreted in the faeces. Dose reductions are recommended for patients with severe liver or kidney disease. Reductions are also required if inhibitors of CYP3A4, such as itraconazole, cannot be avoided. Inducers of CYP3A4, such as phenytoin, should be avoided and St John's wort is contraindicated. Proton pump inhibitors should also be avoided as they reduce pemigatinib concentrations in some patients. As pemigatinib is an inhibitor of P-glycoprotein, doses should be separated by at least six hours from drugs such as digoxin.

A phase II open-label trial studied pemigatinib in 146 previously treated patients with locally advanced or metastatic cholangiocarcinoma. Most (107) of the patients had alterations of FGFR2. After a median follow-up of 17.8 months, 35.5% of this group had a response to treatment. The median duration of the response was 7.5 months with a median progression-free survival of 6.9 months. At the time the trial was published, median overall survival was 21.1 months.[1]

Inhibition of FGFR increases serum phosphate concentrations. In the phase II trial 60% of the patients developed hyperphosphotaemia.[1] This in turn can cause precipitation of calcium crystals and possibly hypocalcaemia, seizures and arrhythmias. Patients may require a low-phosphate diet and phosphate-lowering therapy, but these might need to be discontinued during treatment breaks to avoid hypophosphataemia.

Other very common adverse events during the phase II trial included alopecia, dysgeusia, stomatitis, nausea and diarrhoea.[1] Dry eyes are common and, less frequently, retinal detachment can occur. Regular eye examinations are required. Overall, 9% of the patients stopped treatment because of adverse events, while many others required dose interruptions or reductions.

In animal studies, pemigatinib was toxic to the fetus. Pregnancy should be avoided and male patients should not father a child while taking pemigatinib.

Any benefit of pemigatinib appears to be limited to patients with abnormalities of FGFR2. Although only 2.8% (3/107) of these patients had a complete response, the overall response rate may be better than the response to second-line chemotherapy.[1] Another trial is investigating how pemigatinib would compare to chemotherapy as a first-line treatment for unresectable or metastatic cholangiocarcinoma. At present, pemigatinib is only provisionally approved for previously treated patients with abnormalities of FGFR2. Whether its benefit is sustained, or is reduced by the development of resistance to treatment, requires further study.

T manufacturer provided relevant information

REFERENCES

1. Abou-Alfa GK, Sahai V, Hollebecque A, Vaccaro G, Melisi D, Al-Rajabi R, et al. Pemigatinib for previously treated, locally advanced or metastatic cholangiocarcinoma: a multicentre, open-label, phase 2 study. Lancet Oncol 2020;21:671-84. https://doi.org/10.1016/S1470-2045(20)30109-1

The Transparency Score is explained in New drugs: transparency, Vol 37 No 1, Aust Prescr 2014;37:27.

At the time the comment was prepared, information about this drug was available on the websites of the Food and Drug Administration in the USA and the European Medicines Agency.