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FLT3

FDA grants approval to gilteritinib (Xospata®) for the treatment of relapsed or refractory acute myeloid leukemia with FLT3 mutation

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On 28 November 2018, the US Food and Drug Administration (FDA) granted approval to gilteritinib (Xospata®) for the treatment of adult patients with relapsed or refractory (R/R) acute myeloid leukemia (AML) with a fms like tyrosine kinase 3 (*FLT3*) mutation as detected by an FDA-approved test.[1]

Gilteritinib is a potent, oral *FLT3*/AXL inhibitor, which binds to and inhibits both the wild-type and mutated forms of *FLT3*. Data from a phase I/II dose escalation study (NCT02421939), published in Lancet Oncology (as reported by the AGP) revealed that gilteritinib monotherapy was well tolerated and generated frequent, prolonged, clinically important responses in *FLT3*-mutated R/R AML patients.[2]

The approval by the FDA for gilteritinib is based on data from the ongoing phase III randomized ADMIRAL study (NCT02421939), which is assessing oral gilteritinib 120 mg/day *versus* salvage chemotherapy in adult patients with *FLT3* mutations who are refractory to or have relapsed after first-line AML therapy. The primary endpoints of the study are overall survival (OS) and complete remission/complete remission with partial hematologic recovery (CR/CRh) rates.[4] The design and plan of the phase III ADMIRAL study are discussed by Alexander E. Perl from Abramson Comprehensive Cancer Center, University of Pennsylvania, in an interview with the AGP.

Interim analysis of the phase III ADMIRAL study demonstrated a rate of CR/CRh of 21%, duration of CR/CRh (DOR) of 4.6 months; and the rate of conversion from transfusion dependence to transfusion independence was 31.1% for any 56-day post-baseline period. For patients who achieved a CR/CRh, the median time to first response was 3.6 months (range, 0.9–9.6 months). The CR/CRh rate was 29 of 126 in patients with *FLT3-ITD* or *FLT3-ITD/TKD* and 0 of 12 in patients with FLT3-TKD only.[1]

According to the drug manufacturers, Xospata® is the “first and only FLT3 inhibitor approved by the FDA for patients with relapsed or refractory AML with a *FLT3* mutation.”

References

1. PR Newswire: XOSPATA® (gilteritinib) Approved by U.S. FDA for Adult Patients with Relapsed/Refractory Acute Myeloid Leukemia (AML) with a FLT3 Mutation. 2018 Nov 28. https://www.prnewswire.com/news-releases/xospata-gilteritinib-approved-by-us-fda-for-adult-patients-with-relapsedrefractory-acute-myeloid-leukemia-aml-with-a-flt3-mutation-300757323.html [Accessed 2018 Nov 28].

2. Perl A.E. *et al*. Selective inhibition of FLT3 by gilteritinib in relapsed or refractory acute myeloid leukaemia: a multicentre, first-in-human, open-label, phase 1–2 study. Lancet Oncol. 2017 Jun 20. DOI: 10.1016/S1470-2045(17)30416-3. [Epub ahead of print].

3. Perl A.E. *et al*. An open-label, randomized phase III study of gilteritinib versus salvage chemotherapy in relapsed or refractory FLT3 mutation-positive acute myeloid leukemia. J Clin Oncol. 35, 2017 (suppl; abstr #TPS7067). 2017 American Society of Clinical Oncology (ASCO) Annual Meeting, 2017 June 2–6; Chicago, IL, USA.
