National Community Oncology Dispensing Association, Inc.
PASSION FOR PATIENTS

Written By: Bryan J. Brinda, Pharm.D.
Indiana University Simon Cancer Center
Updated 5/20/19

Positive Quality Intervention: Gilteritinib (XOSPATA) for Relapsed/Refractory Acute Myeloid Leukemia (AML)

Description: This PQI will discuss proper patient selection and management of adverse events related to the administration of oral gilteritinib pharmacotherapy in patients with relapsed/refractory AML that have an FMS-like tyrosine kinase 3 (FLT3) mutation as detected by an FDA-approved test. Optimal dosing and follow-up are essential to help patients benefit fully while taking this medication.

Background: Gilteritinib is a tyrosine kinase inhibitor that has demonstrated activity in patients with relapsed/refractory (R/R) AML who have mutations in the internal tandem duplication (ITD) and/or tyrosine kinase domain (TKD) of FLT3. This represents a treatment paradigm shift as the *first oral option* for this particular subset of AML patients who, if interested in further treatment, would traditionally utilize IV salvage chemotherapy. Clinicians should be aware of the need for molecular re-testing upon relapse and identifying therapy options with the highest level of evidence. In the ADMIRAL study, 21% of patients achieved a complete remission with or without complete hematologic recovery with a median duration of response of 4.6 months (range 0.1-15.8). The median time to respond was 3.6 months and *transfusion-independence* was observed in 31.1% of patients, representing a potential improvement in quality of life.

Common adverse events (all grade >25%):

- Myalgia/arthralgia (42%)
- Transaminase increase (41%)
- Fatigue/malaise (40%)
- Fever (35%)
- Dyspnea (34%)
- Diarrhea (34%)
- Rash (30%)
- Pneumonia (30%)
- Stomatitis (26%)

Rare and serious adverse events:

- Electrocardiogram QT prolonged (7%)
- Posterior reversible encephalopathy syndrome (1%)
- Differentiation syndrome (1%)
- Pancreatitis (Not reported)

Recommended dose adjustments for toxicity:

Adverse Event	Recommended Action
• Posterior reversible encephalopathy syndrome (PRES)	• Discontinue gilteritinib
• QT_c interval > 500 msec	• Interrupt gilteritinib and resume at reduced dose of 80 mg (2 x 40 mg tablets)

	daily when QT_c interval returns to within 30 msec of baseline or ≤ 480 msec
• QT_c interval increased by > 30 msec on ECG on day 8 of cycle 1	• Confirm with ECG on day 9 • If confirmed, consider gilteritinib dose reduction to 80 mg (2 x 40 mg tablets) daily
• Pancreatitis	• Interrupt gilteritinib until pancreatitis is resolved and resume at a reduced dose of 80 mg (2 x 40 mg tablets) daily
• Other grade 3 or higher toxicity (related to treatment)	• Interrupt gilteritinib until toxicity resolves or improves to grade 1 and reduce dose to 80 mg (2 x 40 mg tablets) daily

Gilteritinib is actively being studied in other AML settings including front-line therapy with induction chemotherapy, maintenance therapy after transplant, and in combination with hypomethylators.

PQI Process (upon receipt of new prescription for gilteritinib):

- Ensure that the correct dose is prescribed (3 x 40 mg oral tablets [120 mg total]) by mouth daily
- Ensure that baseline blood counts, chemistries, as well as creatine phosphokinase (CPK) have been assessed prior to initiation of gilteritinib. Schedule these labs for every week for the first month, every other week for the second month, and once monthly thereafter
- Patient should have ECG results prior to initiation of gilteritinib as well as appointments scheduled to receive follow-up ECGs on days 8 and 15 of the first cycle.
- Monitor for any signs/symptoms of pancreatitis, PRES, differentiation syndrome
- Instruct patient to present to nearest emergency department if fever develops
- Consider the use of antidiarrheals
- Important: Upon *refill*, check and clarify dosing, quantity, and instructions to the patient (number of tablets per dose, etc.)

Patient Centered Activities:

- Provide Oncology Chemotherapy Education (OCE) sheet
- Ensure patient knows the appropriate drug dose and schedule (3 x 40 mg oral tablets [120 mg total] once daily continuously)
- Ensure patient knows that the drug may be taken without regard to meals and that the

tablets should not be broken or crushed
- Patients should take their dose as soon as possible if missed on the same day if at least 12 hours before next scheduled dose followed by a return to normal dosing schedule. Patient should not take two doses within 12 hours.
- Counsel female patients of childbearing age to use effective contraception during treatment and for at least six months after the last dose of gilteritinib; male patients should utilize contraception during treatment and for at least 4 months after the last dose of gilteritinib

Co-Pay Assistance

- Patients with commercial paying insurance are eligible for co-pay support
    - Patients pay as little as $0 per prescription
    - Enrollment is for a 12 month period and the program benefit covers up to a maximum of $25,000 per calendar year
    - Contact XOSPATA support solutions (1-844-632-9272) OR your preferred network specialty pharmacy to determine eligibility and enrollment

References:

1. XOSPATA (gilteritinib) [package insert]
2. Perl AE, Altman JK, Cortes J, et al. Selective inhibition of FLT3 by gilteritinib in relapsed or refractory acute myeloid leukaemia: a multicenter, first-in-human, open-label, phase 1-2 study. *Lancet Oncology*. 2017;18(8):1061-1075.
3. Usuki K, Sakura T, Kobayashi Y, et al. Clinical profile of gilteritinib in Japanese patients with relapsed/refractory acute myeloid leukemia: an open-label phase 1 study. *Cancer Science*. 2018;109(10):3235-3244.
4. Perl AE, Cortes JE, Strickland SA, et al. An open-label, randomized phase III study of gilteritinib versus salvage chemotherapy in relapsed or refractory FLT3 mutation-positive acute myeloid leukemia. *Journal of Clinical Oncology*. DOI: 10.1200/JCO.2017.35.15_suppl.TPS7067.