XOSPATA MAY BE THE RIGHT OPTION

for fit patients with R/R FLT3m+ AML like Lucy

WARNING: DIFFERENTIATION SYNDROME

Patients treated with XOSPATA have experienced symptoms of differentiation syndrome, which can be fatal or life-threatening if not treated. Symptoms may include fever, dyspnea, hypoxia, pulmonary infiltrates, pleural or pericardial effusions, rapid weight gain or peripheral edema, hypotension, or renal dysfunction. If differentiation syndrome is suspected, initiate corticosteroid therapy and hemodynamic monitoring until symptom resolution.

INDICATION

XOSPATA is indicated for the treatment of adult patients who have relapsed or refractory acute myeloid leukemia (AML) with a FMS-like tyrosine kinase 3 (FLT3) mutation as detected by an FDA-approved test.

Please see additional Important Safety Information on pages 3-4 and click here for Full Prescribing Information, including BOXED WARNING.

Lucy

58 years old

Mother of 2

Paints in her spare time

Converting bedroom into art studio

Past Medical History

- Casual smoker
- Rheumatoid arthritis
  - Medications: disease-modifying antirheumatic drug and NSAID

AML History

- Primary care physician referred patient to hematologist after patient presented with excessive fatigue. Preliminary lab results revealed abnormal blood counts
- Initial diagnosis of AML determined through bone marrow aspiration and biopsy
- Initial molecular testing conducted at diagnosis found an NPM1 mutation
- Cytogenetics: normal
- ECOG PS: 0
- Risk category (ELN 22): favorable

Current Presentation

Patient presents with high percentage of blasts at follow-up appointment after 4 months of remission following induction and consolidation therapy.

Lab Results

- **WBC:** 44.9 x 10^9/L, 44% blasts
- **Hemoglobin:** 8.7 g/dL
- **Platelet count:** 56.0 x 10^9/L
- **Cytogenetics:** normal
- **ECOG PS:** 0

Molecular Retesting

New FLT3-D835 (*FLT3-TKD*) mutation detected.

AML Treatment History[1]

Induction therapy: 7+3 regimen
consolidation: 4 cycles of HiDAC

Diagnosis

Relapsed AML with presence of a *FLT3-TKD* mutation

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) recommend testing all AML patients for FLT3 mutations at each relapse or disease progression[1]

Gilteritinib (XOSPATA) is the ONLY Category 1 recommendation for patients with relapsed or refractory AML with a FLT3 mutation in the NCCN Guidelines®[1]

AML=acute myeloid leukemia; CBC=complete blood count; CR=complete remission; ECOG PS=Eastern Cooperative Oncology Group Performance Status; ELN=European LeukemiaNet; FLT3=FMS-like tyrosine kinase 3; HiDAC=high-dose cytarabine; m+=mutation-positive; NCCN=National Comprehensive Cancer Network; NPM1=nucleophosmin 1; NSAID=non-steroidal anti-inflammatory drug; PCR=polymerase chain reaction; R/R=relapsed or refractory; TKD=tyrosine kinase domain; WBC=white blood cell.

XOSPATA®
gilteritinib 40mg tablets

XOSPATA delivered superior OS and a higher rate of complete remission* compared with salvage chemotherapy[2†]

XOSPATA is the only targeted monotherapy indicated for the treatment of adult patients with R/R FLT3m+ AML[2,3‡]

36%
reduced risk of death with XOSPATA (n=247)
vs salvage chemotherapy (n=124)
(HR=0.64; 95% CI: 0.49-0.83; *P*=0.0004)[2]

9.3 months
median OS[§] with XOSPATA
(95% CI: 7.7, 10.7)
vs 5.6 months with salvage chemotherapy (95% CI: 4.7, 7.3)[2]

14.2%
CR with XOSPATA
(95% CI: 10.1, 19.2; n=35/247)
vs 10.5% CR with salvage chemotherapy (95% CI: 5.7, 17.3; n=13/124)[2]

Greater median OS was observed with XOSPATA vs salvage chemotherapy[2‖]

XOSPATA (gilteritinib) was evaluated in a Phase 3, open-label, multicenter, randomized clinical trial compared with a prespecified salvage chemotherapy in 371 adult patients with relapsed or refractory FLT3m+ AML.[2,4]

Consider XOSPATA for all of your eligible patients with R/R FLT3m+ AML[2]

*CR was defined as normal marrow differential with <5% blasts, ANC ≥1.0 x 10^9/L and platelets ≥100 x 10^9/L, no evidence of extramedullary leukemia, and must have been RBC and platelet transfusion independent.[2]
†Only responses prior to HSCT were included in the response rate.[2]
‡FLT3 mutation status: *FLT3-ITD*, *FLT3-TKD*, and *FLT3-ITD-TKD*.[2]
§Median overall survival was based on Kaplan-Meier estimates.[5]
‖Exploratory subgroup analysis demonstrated that the hazard ratio for survival was 0.66 (95% CI: 0.47-0.93) for patients in the high-intensity chemotherapy stratum.[2]

AML=acute myeloid leukemia; ANC=absolute neutrophil count; CI=confidence interval; CR=complete remission; FLT3=FMS-like tyrosine kinase 3; HR=hazard ratio; HSCT=hematopoietic stem cell transplant; ITD=internal tandem duplication; m+=mutation-positive; OS=overall survival; RBC=red blood cells; R/R=relapsed or refractory; SC=salvage chemotherapy; TKD=tyrosine kinase domain.

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SELECT SAFETY INFORMATION

CONTRAINDICATIONS

XOSPATA is contraindicated in patients with hypersensitivity to gilteritinib or any of the excipients. Anaphylactic reactions have been observed in clinical trials.

WARNING AND PRECAUTIONS

Posterior Reversible Encephalopathy Syndrome (PRES) 1% of 319 patients treated with XOSPATA in the clinical trials experienced posterior reversible encephalopathy syndrome (PRES) with symptoms including seizure and altered mental status. Symptoms have resolved after discontinuation of XOSPATA. A diagnosis of PRES requires confirmation by brain imaging, preferably magnetic resonance imaging (MRI). Discontinue XOSPATA in patients who develop PRES.

Indication and Important Safety Information

INDICATION

XOSPATA (gilteritinib) is indicated for the treatment of adult patients who have relapsed or refractory acute myeloid leukemia (AML) with a FMS-like tyrosine kinase 3 (FLT3) mutation as detected by an FDA-approved test.

IMPORTANT SAFETY INFORMATION

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WARNINGS AND PRECAUTIONS

Differentiation Syndrome (See BOXED WARNING) 3% of 319 patients treated with XOSPATA in the clinical trials experienced differentiation syndrome. Differentiation syndrome is associated with rapid proliferation and differentiation of myeloid cells and may be life-threatening or fatal if not treated. Symptoms and other clinical findings of differentiation syndrome in patients treated with XOSPATA included fever, dyspnea, pleural effusion, pericardial effusion, pulmonary edema, hypotension, rapid weight gain, peripheral edema, rash, and renal dysfunction. Some cases had concomitant acute febrile neutrophilic dermatosis. Differentiation syndrome occurred as early as 1 day and up to 82 days after XOSPATA initiation and has been observed with or without concomitant leukocytosis. If differentiation syndrome is suspected, initiate dexamethasone 10 mg IV every 12 hours (or an equivalent dose of an alternative oral or IV corticosteroid) and hemodynamic monitoring until improvement. Taper corticosteroids after resolution of symptoms and administer corticosteroids for a minimum of 3 days. Symptoms of differentiation syndrome may recur with premature discontinuation of corticosteroid treatment. If severe signs and/or symptoms persist for more than 48 hours after initiation of corticosteroids, interrupt XOSPATA until signs and symptoms are no longer severe.

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Prolonged QT Interval XOSPATA has been associated with prolonged cardiac ventricular repolarization (QT interval). 1% of the 317 patients with a post-baseline QTc measurement on treatment with XOSPATA in the clinical trial were found to have a QTc interval greater than 500 msec and 7% of patients had an increase from baseline QTc greater than 60 msec. Perform electrocardiogram (ECG) prior to initiation of treatment with XOSPATA, on days 8 and 15 of cycle 1, and prior to the start of the next two subsequent cycles. Interrupt and reduce XOSPATA dosage in patients who have a QTcF >500 msec. Hypokalemia or hypomagnesemia may increase the QT prolongation risk. Correct hypokalemia or hypomagnesemia prior to and during XOSPATA administration.

Pancreatitis 4% of 319 patients treated with XOSPATA in the clinical trials experienced pancreatitis. Evaluate patients who develop signs and symptoms of pancreatitis. Interrupt and reduce the dose of XOSPATA in patients who develop pancreatitis.

Embryo-Fetal Toxicity XOSPATA can cause embryo-fetal harm when administered to a pregnant woman. Advise females of reproductive potential to use effective contraception during treatment with XOSPATA and for 6 months after the last dose of XOSPATA. Advise males with female partners of reproductive potential to use effective contraception during treatment with XOSPATA and for 4 months after the last dose of XOSPATA. Pregnant women, patients becoming pregnant while receiving XOSPATA or male patients with pregnant female partners should be apprised of the potential risk to the fetus.

ADVERSE REACTIONS

Fatal adverse reactions occurred in 2% of patients receiving XOSPATA. These were cardiac arrest (1%) and one case each of differentiation syndrome and pancreatitis. The most frequent (≥5%) nonhematological serious adverse reactions reported in patients were fever (13%), dyspnea (9%), renal impairment (8%), transaminase increased (6%) and noninfectious diarrhea (5%).

7% discontinued XOSPATA treatment permanently due to an adverse reaction. The most common (>1%) adverse reactions leading to discontinuation were aspartate aminotransferase increased (2%) and alanine aminotransferase increased (2%).

The most frequent (≥5%) grade ≥3 nonhematological adverse reactions reported in patients were transaminase increased (21%), dyspnea (12%), hypotension (7%), mucositis (7%), myalgia/arthralgia (7%), and fatigue/malaise (6%).

Other clinically significant adverse reactions occurring in ≤10% of patients included: electrocardiogram QT prolonged (9%), hypersensitivity (8%), pancreatitis (5%), cardiac failure (4%), pericardial effusion (4%), acute febrile neutrophilic dermatosis (3%), differentiation syndrome (3%), pericarditis/myocarditis (2%), large intestine perforation (1%), and posterior reversible encephalopathy syndrome (1%).

Please see additional Important Safety Information on page 4 and click here for Full Prescribing Information, including BOXED WARNING.

Lab Abnormalities Shifts to grades 3-4 nonhematologic laboratory abnormalities in XOSPATA (gilteritinib) treated patients included phosphate decreased (14%), alanine aminotransferase increased (13%), sodium decreased (12%), aspartate aminotransferase increased (10%), calcium decreased (6%), creatine kinase increased (6%), triglycerides increased (6%), creatinine increased (3%), and alkaline phosphatase increased (2%).

DRUG INTERACTIONS

Combined P-gp and Strong CYP3A Inducers Concomitant use of XOSPATA with a combined P-gp and strong CYP3A inducer decreases XOSPATA exposure which may decrease XOSPATA efficacy. Avoid concomitant use of XOSPATA with combined P-gp and strong CYP3A inducers.

Strong CYP3A inhibitors Concomitant use of XOSPATA with a strong CYP3A inhibitor increases XOSPATA exposure. Consider alternative therapies that are not strong CYP3A inhibitors. If the concomitant use of these inhibitors is considered essential for the care of the patient, monitor patient more frequently for XOSPATA adverse reactions. Interrupt and reduce XOSPATA dosage in patients with serious or life-threatening toxicity.

Drugs that Target 5HT2B Receptor or Sigma Nonspecific Receptor Concomitant use of XOSPATA may reduce the effects of drugs that target the 5HT2B receptor or the sigma nonspecific receptor (e.g., escitalopram, fluoxetine, sertraline). Avoid concomitant use of these drugs with XOSPATA unless their use is considered essential for the care of the patient.

P-gp, BCRP, and OCT1 Substrates Based on *in vitro* data, gilteritinib is a P-gp, breast cancer resistant protein (BCRP), and organic cation transporter 1 (OCT1) inhibitor. Coadministration of gilteritinib may increase the exposure of P-gp, BCRP, and OCT1 substrates, which may increase the incidence and severity of adverse reactions of these substrates. For P-gp, BCRP, or OCT1 substrates where small concentration changes may lead to serious adverse reactions, decrease the dose or modify the dosing frequency of such substrate and monitor for adverse reactions as recommended in the respective prescribing information.

SPECIFIC POPULATIONS

Lactation Advise women not to breastfeed during treatment with XOSPATA and for 2 months after the last dose.

Please see Full Prescribing Information including BOXED WARNING for additional safety information.

For important state pricing disclosure information, click **here**.

References: 1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Acute Myeloid Leukemia V.6.2023. © National Comprehensive Cancer Network, Inc. 2023. All rights reserved. Accessed October 24, 2023. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. **2.** XOSPATA [package insert]. Northbrook, IL: Astellas Pharma US, Inc. **3.** Ballesta-López O, Solana-Altabella A, Megías-Vericat JE, Martínez-Cuadrón D, Montesinos P. Gilteritinib use in the treatment of relapsed or refractory acute myeloid leukemia with a FLT3 mutation. Future Oncol. 2021;17(2):215-227. **4.** ClinicalTrials.gov. A study of ASP2215 versus salvage chemotherapy in patients with relapsed or refractory acute myeloid leukemia (AML) with FMS-like tyrosine kinase (FLT3) mutation (03-15-2023). https://clinicaltrials.gov/ct2/show/NCT02421939. Accessed 03-20-2023. **5.** Astellas. XOSPATA. Data on File.

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