You are invited to attend a virtual presentation on:

XOSPATA® (gilteritinib): A Targeted Therapeutic Approach for Relapsed or Refractory *FLT3*m+ AML Patients

Thursday, February 11, 2021
2:00–3:00 PM CT

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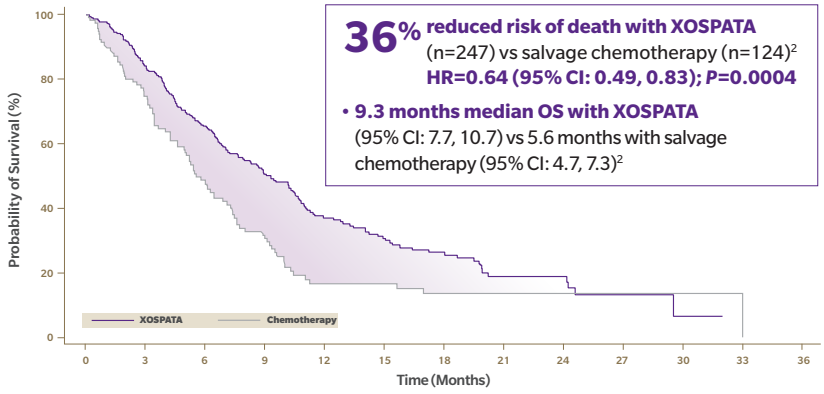
Gilteritinib (XOSPATA) is the ONLY Category 1 recommendation for patients with relapsed or refractory AML with a *FLT3* mutation in the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)[1]

XOSPATA Delivered Superior Overall Survival vs Salvage Chemotherapy in Relapsed or Refractory *FLT3*m+ AML[2*]

Primary Endpoint: Overall Survival[2†]



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

- **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]

Number of Patients at Risk

XOSPATA	247	206	157	106	64	44	31	14	11	4	1	0	0
Chemotherapy	124	84	52	29	13	12	8	7	5	3	1	0	0

XOSPATA was evaluated in a Phase 3, open-label, multicenter, randomized clinical trial compared with a prespecified salvage chemotherapy in adult patients with relapsed or refractory *FLT3*m+ AML.[2,3] Prespecified chemotherapy regimens included high-intensity combinations (MEC[‡] and FLAG-IDA[§]) and low-intensity regimens (LDAC[‖] and AZA[¶]).[2]

1-YEAR SURVIVAL RATE OF XOSPATA VS SALVAGE CHEMOTHERAPY[3¶¶]

37.1% **estimated with XOSPATA** (95% CI: 30.7, 43.6)

16.7% **estimated with salvage chemotherapy** (95% CI: 9.9, 25.0)

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.

Important 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.

**FLT3* mutation status: *FLT3*-ITD, *FLT3*-TKD, and *FLT3*-ITD-TKD.[2]
†The OS endpoint was measured from the date of randomization until death by any cause in the final analysis, which included 371 patients randomized 2:1 to receive XOSPATA or a prespecified salvage chemotherapy regimen.[2]
‡MEC: mitoxantrone 8 mg/m^2, etoposide 100 mg/m^2, and cytarabine 1000 mg/m^2 once daily by IV infusion Days 1 to 5.[2]
§FLAG-IDA: granulocyte colony-stimulating factor 300 mcg/m^2 once daily by SC injection Days 1 to 5, fludarabine 30 mg/m^2 once daily by IV infusion Days 2 through 6, cytarabine 2000 mg/m^2 once daily by IV infusion Days 2 through 6, idarubicin 10 mg/m^2 once daily by IV infusion Days 2 through 4.[2]
‖LDAC: cytarabine 20 mg twice daily by SC injection or IV infusion for 10 days.[2]
¶AZA: azacitidine 75 mg/m^2 once daily by SC injection or IV infusion for 7 days.[2]
¶¶Survival rate and 95% CI were estimated using the Kaplan-Meier method and the Greenwood formula.[3]

AML=acute myeloid leukemia; CI=confidence interval; *FLT3*=FMS-like tyrosine kinase 3; HR=hazard ratio; ITD=internal tandem duplication; IV=intravenous; LDAC=low-dose cytarabine; m+=mutation-positive; NCCN=National Comprehensive Cancer Network; OS=overall survival; SC=subcutaneous; TKD=tyrosine kinase domain.

Please see additional Important Safety Information on the next page.
Please click here for full Prescribing Information including BOXED WARNING.

FOR MORE INFORMATION ABOUT XOSPATA, WE INVITE YOU TO ATTEND THE VIRTUAL PRODUCT THEATER AND VISIT XOSPATAHCP.COM

Important Safety Information (Cont'd)

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 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 2 days and up to 75 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.

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.

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 at least 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 at least 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%).

Lab Abnormalities Shifts to grades 3-4 nonhematologic laboratory abnormalities in XOSPATA 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.

Specific Populations

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

Please click here for full Prescribing Information including BOXED WARNING for additional safety information.

References: 1. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Acute Myeloid Leukemia V.1.2021. © National Comprehensive Cancer Network, Inc. 2020. All rights reserved. Accessed 10-22-2020. 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.** Astellas. XOSPATA. Data on File.

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