

## **Astellas to Present New Data on Gilteritinib in FLT3 Mutation-Positive Acute Myeloid Leukemia at the 2020 American Society of Hematology Annual Meeting**

*Includes five oral presentations that collectively explore the use of gilteritinib across the FLT3mut+ AML care continuum*

**TOKYO, November 16, 2020** – Astellas Pharma Inc. (TSE: 4503, President and CEO: Kenji Yasukawa, Ph.D., “Astellas”) today announced the presentation of new data in acute myeloid leukemia (AML) at the virtual 62<sup>nd</sup> American Society of Hematology (ASH) Annual Meeting and Exposition, taking place December 5-8, 2020.

Nine Astellas-sponsored abstracts focused on patients with AML with a positive FLT3 mutation (FLT3mut+) are being presented, comprising five oral presentations, three posters and one online-only presentation. Oral presentations include new data on the use of gilteritinib, either as monotherapy or in combination, across the FLT3mut+ AML patient spectrum – from those newly diagnosed, to relapsed or refractory patients who have been pre-treated with other tyrosine kinase inhibitors (TKIs) – as well as a secondary analysis of the Phase 3 ADMIRAL trial.

“The research being presented at ASH will shed light on critical unmet needs and continuing progress against AML, which remains a hard-to-treat cancer in spite of continuing medical advances,” said Andrew Krivoschik, M.D., Ph.D., Senior Vice President and Oncology Therapeutic Area Head, Astellas. “Several presentations will describe the effects of gilteritinib in a wide range of AML patients with a positive FLT3 mutation. We also look forward to discussing our Phase 3 LACEWING trial in progress, as well as findings from the STREAMLINE study related to real-world FLT3 testing rates in AML patients, both upon diagnosis and after relapse.”

Gilteritinib is approved as XOSPATA® in the U.S. and selected other countries for the treatment of adult patients who have relapsed or refractory FLT3mut+ AML.

### **Oral Presentations**

**Title:** A Phase 1 Study of Gilteritinib in Combination with Induction and Consolidation Chemotherapy in Patients with Newly Diagnosed AML: Final Results (Abstract 24)

- Presenting author: Dr. Keith W. Pratz, Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University, Baltimore
- Session Date/Time: Saturday, Dec. 5, 7:30 a.m. PST

**Title:** Phase 3, Multicenter, Open-Label Study of Gilteritinib, Gilteritinib Plus Azacitidine, or Azacitidine Alone in Newly Diagnosed FLT3 Mutated (FLT3mut+) Acute Myeloid Leukemia (AML) Patients Ineligible for Intensive Induction Chemotherapy (Trial in progress) (Abstract 27)

- Presenting author: Dr. Eunice S. Wang, Department of Medicine, Roswell Park Comprehensive Cancer Center, Buffalo, N.Y.
- Session Date/Time: Saturday, Dec. 5, 8:15 a.m. PST

**Title:** Comparison of Gilteritinib and Salvage Chemotherapy in FLT3-Mutated Acute Myeloid Leukemia on the Number Needed to Treat for Various Clinical Outcomes: A Secondary Analysis of the ADMIRAL Trial (Abstract 213)

- Presenting author: Amer M. Zeidan, Yale University School of Medicine and Yale Cancer Center, New Haven, Conn.
- Session Date/Time: Saturday, Dec. 5, noon PST

**Title:** Efficacy and Safety of Venetoclax in Combination with Gilteritinib for Relapsed/Refractory FLT3 Mutated Acute Myeloid Leukemia in the Expansion Cohort of a Phase 1b Study (Abstract 333) (Supported by AbbVie, Astellas and Genentech)

- Presenting author: Dr. Naval G. Daver, Department of Leukemia, The University of Texas MD Anderson Cancer Center, Houston
- Session Date/Time: Sunday, Dec. 6, 10:15 a.m. PST

**Title:** Clinical Outcomes in Patients with Relapsed/Refractory Acute Myeloid Leukemia Treated with Gilteritinib Who Received Prior Midostaurin or Sorafenib (Abstract 334)

- Presenting author: Dr. Alexander E. Perl, Abramson Cancer Center, University of Pennsylvania, Philadelphia
- Session Date/Time: Sunday, Dec. 6, 10:30 a.m. PST

### **Poster Presentations**

Poster presentations are available online from Saturday, Dec. 5, 7 a.m. PST to Monday, Dec. 7, 3:30 p.m. PST.

**Title** STREAMLINE – Retrospective Cohort Study of Relapsed or Refractory (R/R) FLT3-Mutated Acute Myeloid Leukemia (AML): Real-World Treatment, Testing Patterns, and Outcomes (Abstract 2826)

- Presenting author: Dr. Amer M. Zeidan, Yale University School of Medicine and Yale Cancer Center, New Haven, Conn.

**Title:** Clinical Outcomes Following Treatment with Gilteritinib or Quizartinib in Patients with Relapsed/Refractory FLT3-ITD+ Acute Myeloid Leukemia (Abstract 995)

- Presenting author: Dr. Alexander E. Perl, Abramson Cancer Center, University of Pennsylvania, Philadelphia

**Title:** Pain and Opioid Use in Patients with FLT3 Mutation-Positive Relapsed/Refractory AML: A Subanalysis of Patient-Reported Outcomes from the ADMIRAL Trial (Abstract 2568)

- Presenting author: Manasee V. Shah, Global Health Economics and Outcomes Research, Astellas

### **Online-Only Presentation**

**Title:** Real-World Use of FLT3-TKIs in R/R FLT3-Mutated AML in the United States (Abstract 4413)

## Astellas-Supported Satellite Symposium

Astellas will support the following pre-meeting Friday Satellite Symposia Live Webinar.

### Title: Consensus or Controversy? Investigators Discuss Clinical Practice Patterns and Available Research Data Guiding the Management of Acute Myeloid Leukemia (Part 3 of a 4-part Series)

- Session Date/Time: Friday, Dec. 4, 3-6 p.m. PST

#### About Gilteritinib

Gilteritinib was discovered through a research collaboration with Kotobuki Pharmaceutical Co., Ltd., and Astellas has exclusive global rights to develop, manufacture and commercialize gilteritinib. Gilteritinib is available as XOSPATA® in the U.S., Japan and selected European countries, among others, for the treatment of adult patients who have relapsed or refractory FLT3mut+ AML.<sup>1</sup> Gilteritinib is an FMS-like tyrosine kinase 3 (FLT3) inhibitor with demonstrated activity against FLT3-ITD, a common driver mutation that presents with a high burden and poor prognosis, and FLT3-TKD mutations.<sup>2</sup>

#### About XOSPATA® (gilteritinib) in the United States

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

#### Important Safety Information

##### **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.

#### Contraindications

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

#### 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 ( $\geq 5\%$ ) 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 ( $\geq 5\%$ ) grade  $\geq 3$  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  $\leq 10\%$  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 see **Full Prescribing Information** including **BOXED WARNING** for additional safety information.

#### **About Astellas**

Astellas Pharma Inc., is a pharmaceutical company conducting business in more than 70 countries around the world. We are promoting the Focus Area Approach that is designed to identify opportunities for the continuous creation of new drugs to address diseases with high unmet medical needs by focusing on Biology and Modality. Furthermore, we are also looking beyond our foundational Rx focus to create Rx+<sup>®</sup> healthcare solutions that combine our expertise and knowledge with cutting-edge technology in different fields of external partners. Through these efforts, Astellas stands on the forefront of healthcare change to turn innovative science into value for patients. For more information, please visit our website at <https://www.astellas.com/en>.

#### **Cautionary Notes**

In this press release, statements made with respect to current plans, estimates, strategies and beliefs and other statements that are not historical facts are forward-looking statements about the future performance of Astellas. These statements are based on management's current assumptions and beliefs in light of the information currently available to it and involve known and unknown risks and uncertainties. A number of factors could cause actual results to differ materially from those discussed in the forward-looking statements. Such factors include, but are not limited to: (i) changes in general economic conditions and in laws and regulations, relating to pharmaceutical markets, (ii) currency exchange rate fluctuations, (iii) delays in new product launches, (iv) the inability of Astellas to market existing and new products effectively, (v) the inability of Astellas to continue to effectively research and develop products accepted by customers in highly competitive markets, and (vi) infringements of Astellas' intellectual property rights by third parties.

Information about pharmaceutical products (including products currently in development) which is included in this press release is not intended to constitute an advertisement or medical advice.

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#### **References**

1. Data on file. Northbrook, IL: Astellas Pharma Inc.
2. Daver N, Schlenk RF, Russel NH, Levis MJ. (2019). Targeting FLT3 mutations in AML: review of current knowledge and evidence. *Leukemia* 33: 299-312.
3. XOSPATA [package insert]. Northbrook, IL: Astellas Pharma Inc.