Press release

Astellas Receives Positive CHMP Opinion for XOSPATA® (gilteritinib) as a Monotherapy for Patients with Relapsed or Refractory Acute Myeloid Leukemia with a FLT3 Mutation

If approved by the European Commission, gilteritinib would represent one of the few advances in Europe for AML over the past 40 years[1]

TOKYO, Sept. 20, 2019 – Astellas Pharma Inc. (TSE: 4503, President and CEO: Kenji Yasukawa, Ph.D., "Astellas") announced today that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has adopted a positive opinion recommending the oral once-daily therapy XOSPATA® (gilteritinib) as a monotherapy for the treatment of adult patients who have relapsed or refractory (resistant to treatment) acute myeloid leukemia (AML) with a FLT3 mutation (FLT3mut+).[2] If approved by the European Commission (EC), gilteritinib has the potential to improve treatment outcomes for AML patients with the most common mutations – FLT3 internal tandem duplication (ITD) and FLT3 tyrosine kinase domain (TKD) – and would be one of the few advances for the treatment of AML in Europe over the past 40 years.[1,3] Gilteritinib received accelerated assessment from the EMA, which allowed the CHMP to reduce the timeframe for approval.[4]

"The data are encouraging, showing a significant improvement in overall survival (OS), and one-year survival rates doubled when comparing gilteritinib to the current standard of care," said Giovanni Martinelli, M.D., Institute of Hematology, S.Orsola-Malpighi University Hospital, Bologna, Italy, a study investigator. "For relapsed or refractory FLT3mut+ AML patients the current prognosis is poor, with median OS of less than six months following treatment with salvage chemotherapy. If approved by the EC, gilteritinib has the potential to change the treatment landscape."

The CHMP decision is based on results from the Phase 3 ADMIRAL trial, which investigated gilteritinib versus salvage chemotherapy in patients with relapsed or refractory FLT3mut+ AML.[5] Patients treated with gilteritinib had significantly longer OS than those who received salvage chemotherapy.[5] Median OS for patients who received gilteritinib was 9.3 months, compared to 5.6 months for patients who received salvage chemotherapy (Hazard Ratio = 0.64 (95% CI 0.49, 0.83), P=0.0004).[5,6] Rates of one-year survival were 37% for patients who received gilteritinib, compared to 17% for patients who received salvage chemotherapy.[5]

"There is a high unmet need in AML and Astellas is committed to improving treatment options. Gilteritinib offers a potential new alternative for patients with relapsed or refractory FLT3mut+ AML, with data showing improved survival outcomes," said Andrew Krivoshik, M.D., Ph.D., Senior Vice President and Global Therapeutic Area Head, Oncology Development, Astellas. "Subject to EC approval, gilteritinib has the potential to provide new hope for clinicians, patients and their families."

The positive opinion from the CHMP will now be reviewed by the EC, which has the authority to approve medicines for the 28 European Union member countries, and is also valid in Iceland, Norway and Liechtenstein.[7] In late 2018, gilteritinib was approved by regulatory agencies in the U.S. and Japan for the treatment of adult patients who have relapsed or refractory FLT3mut+ AML.[8,9]

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. Last year gilteritinib received an Orphan Designation from the European Commission and received accelerated assessment from the EMA.[4,10]

In the U.S., gilteritinib was previously granted Orphan Drug Designation and Fast Track Designation by the Food and Drug Administration (FDA), and was approved in November 2018 for the treatment of adult patients with relapsed or refractory FLT3mut+ AML, based on interim complete remission/complete remission with partial hematologic recovery (CR/CRh) data from the Phase 3 ADMIRAL trial.[8] Gilteritinib has also received approval for a supplemental New Drug Application (sNDA) from the FDA, adding Overall Survival (OS) data from the Phase 3 ADMIRAL trial in relapsed or refractory FLT3mut+ AML to the gilteritinib label.[6] Full results from the ADMIRAL trial were presented at the American Association for Cancer Research (AACR) Annual Meeting in April 2019.[5]

In Japan, gilteritinib received Orphan Drug Designation and SAKIGAKE Designation from the Japanese Ministry of Health, Labour and Welfare and was approved for the treatment of adult patients with relapsed or refractory FLT3mut+ AML in September 2018.[9,11] In August 2019, the Japanese package insert for gilteritinib was revised to include information regarding OS data from the ADMIRAL trial.[12]

Astellas is currently investigating gilteritinib in various FLT3mut+ AML patient populations through several Phase 3 trials.

About the ADMIRAL Trial[13]
The Phase 3 ADMIRAL trial (NCT02421939) was an open-label, multicenter, randomized study of gilteritinib versus salvage chemotherapy in adult patients with FLT3mut+ who are refractory to or have relapsed after first-line AML therapy. The co-primary endpoints of the trial were OS and CR/CRh rates. The study enrolled 371 patients with relapsed or refractory AML and FLT3mut+ present in bone marrow or whole blood. Subjects were randomized in a 2:1 ratio to receive gilteritinib (120 mg[5]) or salvage chemotherapy.

The most common adverse events (AEs) across both treatment arms of the ADMIRAL trial were febrile neutropenia (43.7%), anemia (43.4%), and pyrexia (38.6%).[5] Common grade ≥3 AEs related to gilteritinib were anemia (19.5%), febrile neutropenia (15.4%), thrombocytopenia (12.2%), and decreased platelet count (12.2%).[5] Adjusted for exposure duration, serious treatment-emergent AEs per patient year were less common with gilteritinib (7.1%) than salvage chemotherapy (9.2%).[5]

About Astellas
Astellas Pharma Inc., based in Tokyo, Japan, is a company dedicated to improving the health of people around the world through the provision of innovative and reliable pharmaceutical products. 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.

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