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Submission Request
National Comprehensive Cancer Network® (NCCN)

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NCCN Guidelines Panel:	Acute Myeloid Leukemia Panel

To Whom It May Concern:

On behalf of Astellas Pharma Inc., we respectfully request the NCCN Acute Myeloid Leukemia (AML) Panel to review and consider the inclusion of the enclosed data for gilteritinib, a FMS-like tyrosine kinase-3 (FLT3) inhibitor, into the guidelines for FLT3 mutation positive (FLT3m+) AML.

Specific Changes:

In consideration with the FDA approval of gilteritinib, a FLT 3 inhibitor, and the FDA approved prescribing information, please consider gilteritinib as a category 1 recommendation for relapsed or refractory AML. In addition, new data for gilteritinib use in newly diagnosed AML patients is enclosed; please consider inclusion in the guidelines.

FDA Clearance:

Gilteritinib is FDA approved for the treatment of relapsed or refractory AML in patients with a FLT3 mutation as detected by an FDA-approved test. Gilteritinib is not FDA approved for patients with newly diagnosed disease.

Rationale:

This submission is based on the positive interim results from the ADMIRAL trial (NCT02421939), a study of gilteritinib versus salvage chemotherapy in patients with Relapsed or Refractory Acute Myeloid Leukemia with FLT3 mutation; the findings from the safety cohort of the ongoing LACEWING trial (NCT02752035), a Multicenter, Open-label, 3- Arm Study of Gilteritinib, Gilteritinib plus Azacitidine, or Azacitidine Alone in Newly Diagnosed FLT3 Mutated Acute Myeloid Leukemia Patients Ineligible for Intensive Induction Chemotherapy; and the Updated Results from a Phase 1 Study of Gilteritinib In Combination with Induction and Consolidation Chemotherapy in Subjects with Newly Diagnosed Acute Myeloid Leukemia. The latter two ongoing studies have been presented at the American Society of Hematology Annual Meeting 2018 .[1-3]

The ADMIRAL trial (NCT02421939) interim analysis included 138 patients with relapsed or refractory AML to first line of treatment and included patients with FLT3-ITD, D835 and I836 mutations.[1] The trial established interim efficacy by the complete remission (CR)/complete remission with partial hematologic recovery (CRh), duration of CR/CRh (DOR) and rate of conversion from transfusion dependence to transfusion independence. The trial found CR/CRh rate to be 21%. Median DOR was 4.6 months and 33 patients of 106 (31.1%) became transfusion independent that were previously dependent on red blood cell and/or platelet transfusions at baseline.

The LACEWING trial (NCT02752035) and Updated Results from a Phase 1 Study of Gilteritinib in Combination with Induction and Consolidation Chemotherapy in Subjects with Newly Diagnosed Acute Myeloid Leukemia (NCT02236013) were both presented at the American Society of Hematology Annual Meeting 2018 and are currently ongoing. Both trials are focused on patients in the newly diagnosed setting, in patients unable to receive intensive chemotherapy and in combination with intensive chemotherapy, respectively.[2,3]

We appreciate your review and consideration for inclusion in the NCCN guidelines. Please let us know of any questions.

Sincerely,

Steven Sesterhenn, MD, MBA
Medical Director, Medical Affairs Americas

Reference List

1. XOSPATA [package insert]. Northbrook, IL, USA: Astellas Pharma US, Inc.

2. Esteve J, Schots R, Del Bernal Castillo T, et al. Multicenter, Open-Label, 3-Arm 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: Findings From the Safety Cohort [abstract]. *Blood*. 2018.

3. Keith W. Pratz MD, Mohamad Cherry M, M.S., Jessica K. Altman MD, et al. Updated Results from a Phase 1 Study of Gilteritinib in Combination with Induction and Consolidation Chemotherapy in Subjects with Newly Diagnosed Acute Myeloid Leukemia (AML) [abstract]. *Blood*. 2018.