April 13, 2018

Submission Request
National Comprehensive Cancer Network® (NCCN)


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| Name: | Laura Elise Horvath, MD |
| Company/Organization: | Astellas Pharma Inc. |
| Address: | 1 Astellas Way<br>Northbrook, IL 60062 |
| Phone: | 847-226-2047 |
| Email: | laura.horvath@astellas.com |
| Date of request: | April 13, 2018 |
| 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) and AXL inhibitor, into the guidelines for the treatment of FLT3 mutation positive (FLT3m+) AML.

Specific Changes:

Please consider inclusion of gilteritinib, a FLT3 inhibitor and AXL inhibitor, into the guidelines for the treatment of AML based on available data.

FDA Clearance:

Gilteritinib does not have FDA approval for the treatment of AML.

Rationale:

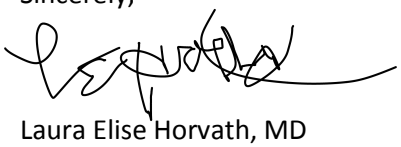
This submission is based on the positive results from two studies: the Phase 1/2 CHRYSALIS trial of gilteritinib in relapsed or refractory AML and Preliminary Results from a Phase 1 study of Gilteritinib in Combination with Induction and Consolidation Chemotherapy in Subjects with Newly Diagnosed AML presented at the American Society of Hematology Annual Meeting 2017.[1,2]

CHRYSALIS was a Phase 1/2 study evaluating safety, tolerability, pharmacokinetic and anti-leukemic activity of gilteritinib in patients with relapsed or refractory AML.[1] Patients in CHRYSALIS tolerated gilteritinib therapy and showed consistent FLT3 inhibition at doses greater than or equal to 80 milligrams (mg) per day. The authors reported a 55% objective response rate (ORR) in patients with FLT3 internal tandem duplication (ITD) mutations and a median overall survival (OS) at about 31 weeks (95% CI: 24-35). Treatment related adverse events reported in ≥10% of patients in the safety population included diarrhea (16%), fatigue (13%), aspartate aminotransferase (AST) increase (12%) and grade 3 ≥ QTc prolongation was reported in 3% of subjects.

The Preliminary Results from the Phase 1 study of Gilteritinib in Combination with Induction and Consolidation Chemotherapy in Subjects with Newly Diagnosed Acute Myeloid Leukemia (AML) were reported by Dr. Keith Pratz at the 2017 American Society of Hematology Annual Meeting. Interim study results regarding safety, tolerability and anti-tumor activity of gilteritinib in the newly diagnosed setting with intensive chemotherapy were presented. Median duration of response and OS have not yet been reported. Forty-nine of the 50 enrolled subjects were evaluated; in FLT3 mutant patients, the composite complete remission rate (CRc) was 91.3% and 56% in FLT3 mutation negative patients at the time of analysis. The authors reported that gilteritinib was well tolerated and grade ≥ 3 treatment-emergent adverse events occurring in ≥ 10% of patients included febrile neutropenia (53.1%), thrombocytopenia (18.4%), neutropenia (16.3%), decreased platelet count (12.2%), sepsis (10.2%), and decreased white blood cell count (10.2%). Serious drug related treatment-emergent adverse events occurring in >1 subject were febrile neutropenia (16.3%), sepsis (6.1%), and decreased ejection fraction (4.1%).

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

Sincerely,



Laura Elise Horvath, MD

Medical Director, Medical Affairs

Reference List and Supporting Literature


1. Perl AE, Altman JK, Cortes J, et al. Selective inhibition of FLT3 by gilteritinib in relapsed or refractory acute myeloid leukaemia: a multicentre, first-in-human, open-label, phase 1-2 study. *Lancet Oncol*. 2017;18(8):1061-1075. Available at: https://dx.doi.org/10.1016/S1470-2045(17)30416-3.

2. Pratz K, Cherry M, Altman JK, et al. Preliminary 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]. 2017 Abstract # 722. Available at: https://ash.confex.com/ash/2017/webprogram/Paper104989.html.