Long-term Survivors and Gilteritinib Safety Beyond 1 Year in *FLT3*-Mutated R/R AML: ADMIRAL Trial Follow-up

Alexander E. Perl[1]; Giovanni Martinelli[2]; Andreas Neubauer[3]; Ellin Berman[4]; Maria R. Baer[5]; Richard A. Larson[6]; Amir T. Fathi[7]; Hisayuki Yokoyama[8]; Naoko Hosono[9]; Nahla Hasabou[10]; Qiaoyang Lu[10]; Erkut Bahceci[10]

[1]Abramson Cancer Center, University of Pennsylvania, Philadelphia, PA; [2]Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST) IRCCS, Meldola, Italy; [3]Universitätsklinikum Giessen und Marburg GmbH, Marburg, Germany; [4]Memorial Sloan Kettering Cancer Center, New York, NY; [5]University of Maryland Greenebaum Comprehensive Cancer Center, Baltimore, MD; [6]University of Chicago, Chicago, IL; [7]Massachusetts General Hospital, Harvard Medical School, Boston, MA; [8]*Sendai Medical Center, National Hospital Organization, Sendai, Japan; [9]University of Fukui, Fukui, Japan; [10]Astellas Pharma US, Inc., Northbrook, IL

*Indicates former affiliation where work was performed; the current affiliation is Tohoku University, Sendai, Japan.

Introduction: The phase 3 ADMIRAL trial showed that gilteritinib was superior to salvage chemotherapy (SC) in *FLT3*$^{mut+}$ R/R AML patients (Perl AE, et al. *N Engl J Med*. 2019). This follow-up of the ADMIRAL trial assessed long-term survivors and gilteritinib safety beyond 1 year.

Methods: A data cut was performed 1 year after the primary analysis. Response outcomes in long-term survivors (OS ≥18 months) in the gilteritinib arm, and safety during and after 12 months of gilteritinib therapy were assessed.

Results: At 1 year after the primary analysis, median follow-up for OS was 29.2 months. Median OS remained longer with gilteritinib (9.3 months) than with SC (5.6 months; HR=0.679 [95% CI: 0.527, 0.875], nominal *P*=0.0026); 18-month OS rates were 27% and 15%, respectively (**Table**). Of 49 censored patients in the gilteritinib arm, 20 continued treatment; 13 of these 20 patients underwent transplantation (HSCT) and received gilteritinib post-HSCT. Median gilteritinib exposure was 4.1 months (IQR, 2.1-8.2); 12% (n=30/246) of patients had ≥18 months of drug exposure.

A total of 63 gilteritinib-treated patients had OS ≥18 months (median exposure, 17.6 months [IQR, 3.1-25.7 months]). A high proportion of these long-term survivors achieved remission pre-HSCT (**Table**). After a median of 3.5 months, 35 of 63 (56%) long-term survivors underwent HSCT; 25 of these 35 patients (71%) received post-HSCT gilteritinib therapy. Of 28 patients who did not undergo HSCT, 15 (54%) received gilteritinib for ≥18 months.

Most common grade ≥3 adverse events (AEs) during the first 12 months of gilteritinib therapy were febrile neutropenia (45%), anemia (40%), and thrombocytopenia (23%); rates of these grade ≥3 AEs decreased to 8%, 10%, and 0, respectively, after 12 months of treatment. Most common fatal AEs during the first 12 months of gilteritinib therapy were AML (11%), infections (11%), and cardiac disorders (3%); after 12 months of treatment, rates of these fatal AEs were 6%, 8%, and 2%, respectively.

Conclusion: Results from this ADMIRAL trial follow-up suggest long-term survival in patients receiving gilteritinib is related to ongoing remission, subsequent HSCT, or post-HSCT gilteritinib therapy. The safety profile of gilteritinib beyond 1 year was stable.

	Gilteritinib (n=247)	**SC (n=124)**
Deaths, n (%)	198 (80%)	94 (76%)
OS Rates (%)		
12-month	37	19
18-month	27	15
24-month	20	14
Pre-HSCT Remission Rates in Gilteritinib Long-term Survivors (n=63), n (%)		
CR	20 (32)	
CRi/CRp	25 (40)	
CRc*	**45 (71)**	
CRh	10 (16)	
CR/CRh	**30 (48)**	

Bold font indicates aggregate responses.
*Defined as the sum of patients who achieved CR, CRi, and CRp.
Abbreviations: CR, complete remission; CRc, composite complete remission; CRh, complete remission with partial hematologic recovery CRi, complete remission with incomplete hematologic recovery; CRp, complete remission with incomplete platelet recovery; HSCT, hematopoietic stem cell transplantation; OS, overall survival; SC, salvage chemotherapy.

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