Supplementary Materials for:

Early initiation of low-dose gilteritinib maintenance improves post-transplant outcomes in patients with R/R FLT3^{mut} AML

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This file includes:

Supplemental method

Supplemental figure 1 and 2

Supplemental Table 1

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Supplemental method

We retrospectively analyzed 25 cases with FLT3-mutated AML who received allogeneic SCT at our center between January 1, 2011, and April 30, 2022. They were observed till June 30, 2022. FLT3 mutation was analyzed using a polymerase chain reaction (PCR)-based assay (ITD and TKD mutation by LeukoStrat CDx after 2018 and ITD mutation by in-house PCR before 2018).

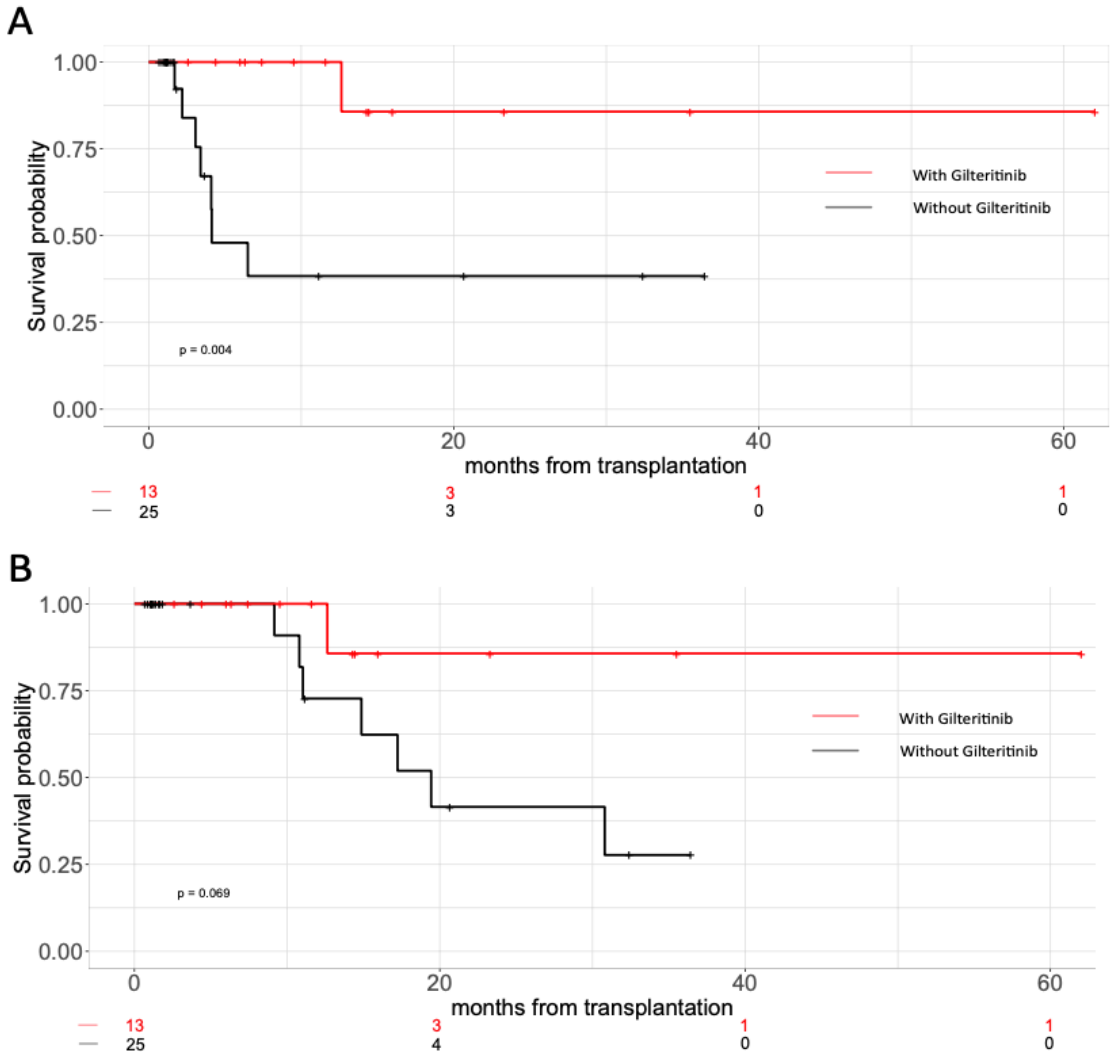
Relapse was defined as a reappearance of leukemic blasts in the peripheral blood or ≥ 5% blasts in the bone marrow[1]. Non-relapse mortality (NRM) was defined as death without relapse. Relapse-free survival (RFS) was defined as the time from transplantation to leukemia relapse or death from any cause. Overall survival (OS) was defined as the time from transplantation to death due to any cause. Patients with no events reported at the time of analysis were censored on June 30, 2022.

Baseline characteristics were compared between patients with and without gilteritinib treatment, using the Mann–Whitney U-test or Student's *t*-test for continuous variables and the Fisher exact test for categorical variables. Measurable residual disease (MRD) was evaluated by combining Wilms' tumor 1 (WT1)-mRNA expression in the peripheral blood and multicolor flow cytometry in the bone marrow. WT1-mRNA was considered negative when less than 50 copies/μg. MRD was measured on days 28-45 after SCT. RFS and OS were estimated using the Kaplan–Meier method and compared using the log-rank test. Moreover, one-year RFS and OS rates with 95% confidence intervals (CIs) were determined. Cumulative incidences were used to calculate the rate of relapse and compared using Gray's test. The competing event for relapse was the NRM. Acute and chronic graft-versus-host disease (GVHD) were graded according to previously published criteria[2,3]. Death or relapse before GVHD onset was a competing risk. All statistical analyses were performed using R-software (version 3.6.1, The R Foundation for Statistical Computing, Vienna, Austria) in R-Studio. A two-sided $p < 0.05$ was considered statistically significant.

References

1. Cheson BD, Bennett JM, Kopecky KJ, et al. Revised Recommendations of the International Working Group for Diagnosis, Standardization of Response Criteria, Treatment Outcomes, and Reporting Standards for Therapeutic Trials in Acute Myeloid Leukemia. *Journal of Clinical Oncology*. 2003;21(24):4642-4649.
2. Przepiorka D, Weisdorf D, Martin P, et al. 1994 Consensus Conference on Acute GVHD Grading. *Bone Marrow Transplant*. 1995;15(6):825-828.
3. Jagasia MH, Greinix HT, Arora M, et al. National Institutes of Health Consensus Development Project on Criteria for Clinical Trials in Chronic Graft-versus-Host Disease: I. The 2014 Diagnosis and Staging Working Group report. *Biol Blood Marrow Transplant*. 2015;21(3):389-401.e381

Supplemental Figure 1

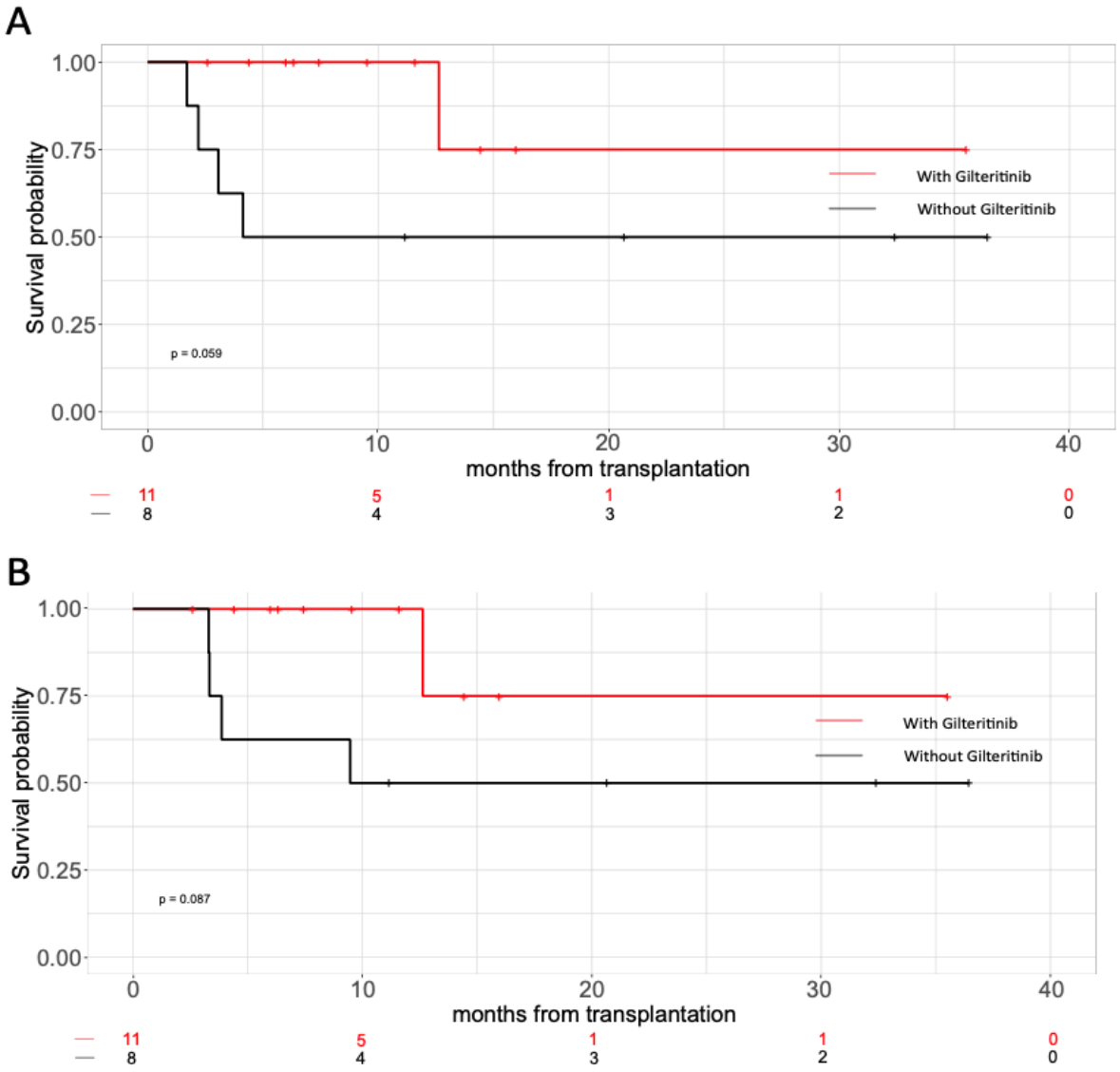


Supplemental Figure 1. Time-dependent covariate hazard model

A: RFS from transplantation by using time-dependent covariate hazard model (HR: 0.089, *p* = 0.004)

B: OS from transplantation by using time-dependent covariate hazard model (HR: 0.20, *p* = 0.069)

Supplemental Figure 2



Supplemental Figure 2. Analysis only in patients with 1st SCT

A: RFS from transplantation only in patients with 1st SCT (n = 19, 1-year RFS; 100% in gilteritinib group vs. 50% in non-gilteritinib group, *p* = 0.059)

B: OS from transplantation only in patients with 1st SCT (n = 19, 1-year OS; 100% in gilteritinib group vs. 50% in non-gilteritinib group, *p* = 0.087)

Supplemental Table 1.
Adverse events that caused temporary withdrawal of gilteritinib

	number
Hematological	
Thrombocytopenia	3
Neutropenia	2
Anemia	1
Non-hematological	
Acute GVHD	2
Chronic GVHD	1
Sepsis	1
Fever	1
General fatigue	1
Duodenum ulcer	1
Increased CPK	1

Abbreviations: CPK; creatine phosphorus kinase, GVHD; graft-versus-host disease