Supplementary information for

Superior Response and Survival of Intensive Chemotherapy Over Venetoclax Plus Azacitidine in Newly Diagnosed KIT-Mutated Acute Myeloid Leukemia

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A. List of Abbreviations

AML	acute myeloid leukemia
IC	Intensive Chemotherapy
VA	Venetoclax plus Azacitidine
EFS	Event-Free Survival
OS	Overall Survival
CR	Complete Remission
ORR	Overall Response Rate
MRD	Minimal Residual Disease
PSM	Propensity Score Matching
ELN	European LeukemiaNet
FAB	French-American-British
ECOG	Eastern Cooperative Oncology Group
HR	Hazard Ratio
CI	Confidence Interval
allo-HSCT	Allogeneic Hematopoietic Stem Cell Transplantation

B. Supplementary Table

Table S1. Spectrum and Distribution of KIT Mutations in 67 Patients with KIT-Mutated AML

KIT mutation	Number of Mutation Events	Percentage (%)
Exon 17	53	79.10
D816V	35	66.04
D816Y	5	9.43
D816H	3	5.66
N822K	17	32.08
Other exon 17	1	1.89
Exon 8	14	20.90
Other exons	5	7.46

This table details the distribution of specific KIT mutations identified in the study cohort of 67 KIT-mutated AML patients. As some patients harbored multiple KIT mutations, the total number of mutational events exceeds the number of patients. Mutations are categorized by exon location, with exon 17 mutations further subdivided by specific amino acid changes. The D816V variant was the most prevalent. Percentages for individual exon 17 mutations are calculated relative to the total number of patients with exon 17 mutations (n=53), while all other percentages are calculated relative to the total KIT-mutated cohort (n=67).

Table S2. Impact of allo-HSCT on Survival in VA-Treated Patients

A. Time-Dependent Cox Regression Analysis

Outcome	HR (95% CI)	P-value
OS	0.11 (0.02–0.77)	0.027
EFS	0.09 (0.01–0.62)	0.015

B. Landmark Sensitivity Analysis

Landmark Time (months)	P-value	Total Patients	Transplanted Patients
4	0.589	146	1
6	0.089	137	9
8	0.022	121	13

C. Cohort Characteristics

Characteristic	Number of Patients
Total cohort	172
Transplanted	14
Non-transplanted	158
6-month landmark cohort	137

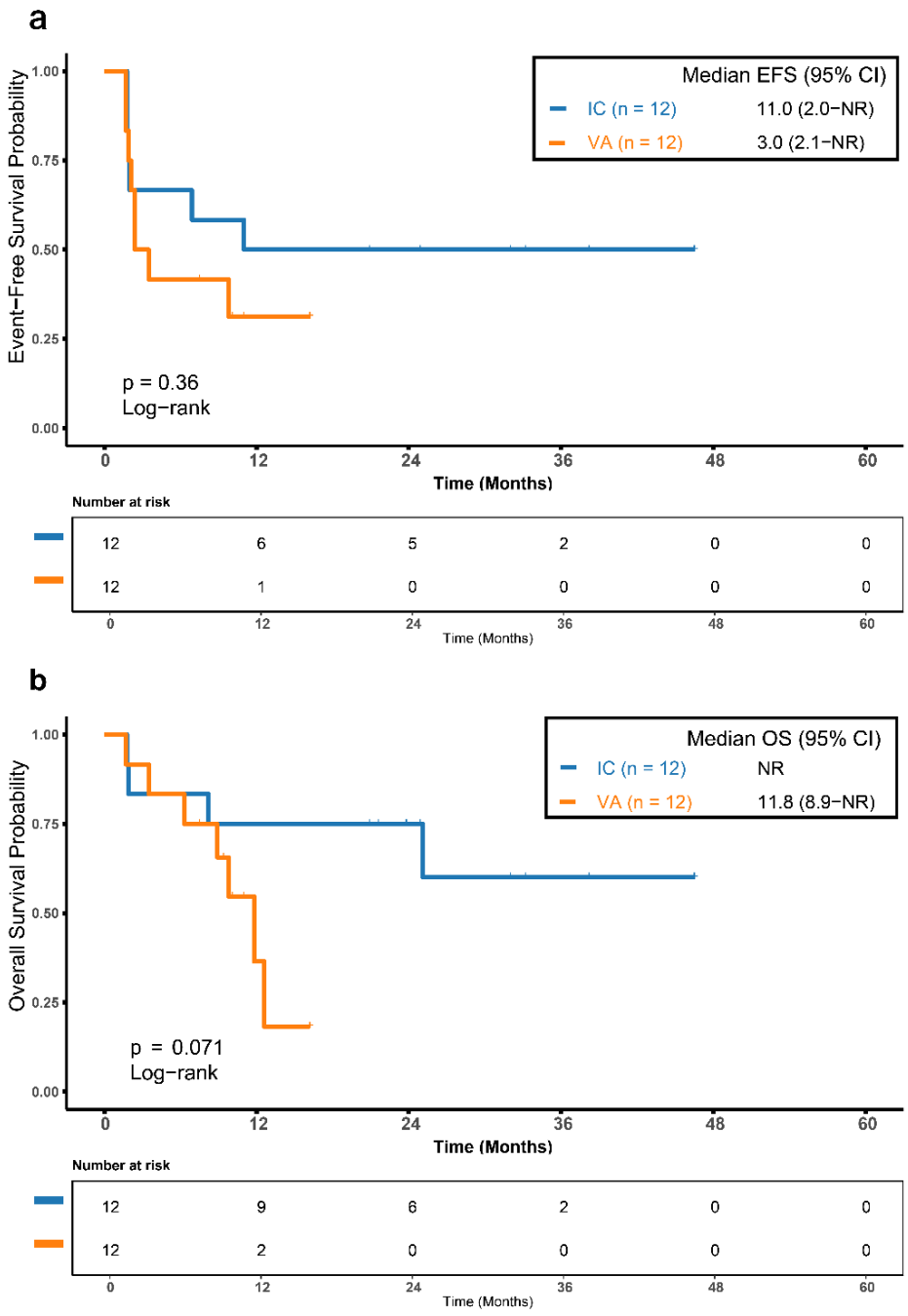
Analysis of allo-HSCT impact using time-dependent Cox regression to account for immortal time bias. The time-dependent analysis treated transplantation as a time-varying covariate. Landmark analyses were performed as sensitivity analyses at multiple time points.

C. Supplementary Figures

Figure S1. Survival After PSM: IC vs VA in KIT-Mutated AML

(a) EFS in the matched cohorts.

(b) OS in the matched cohorts.

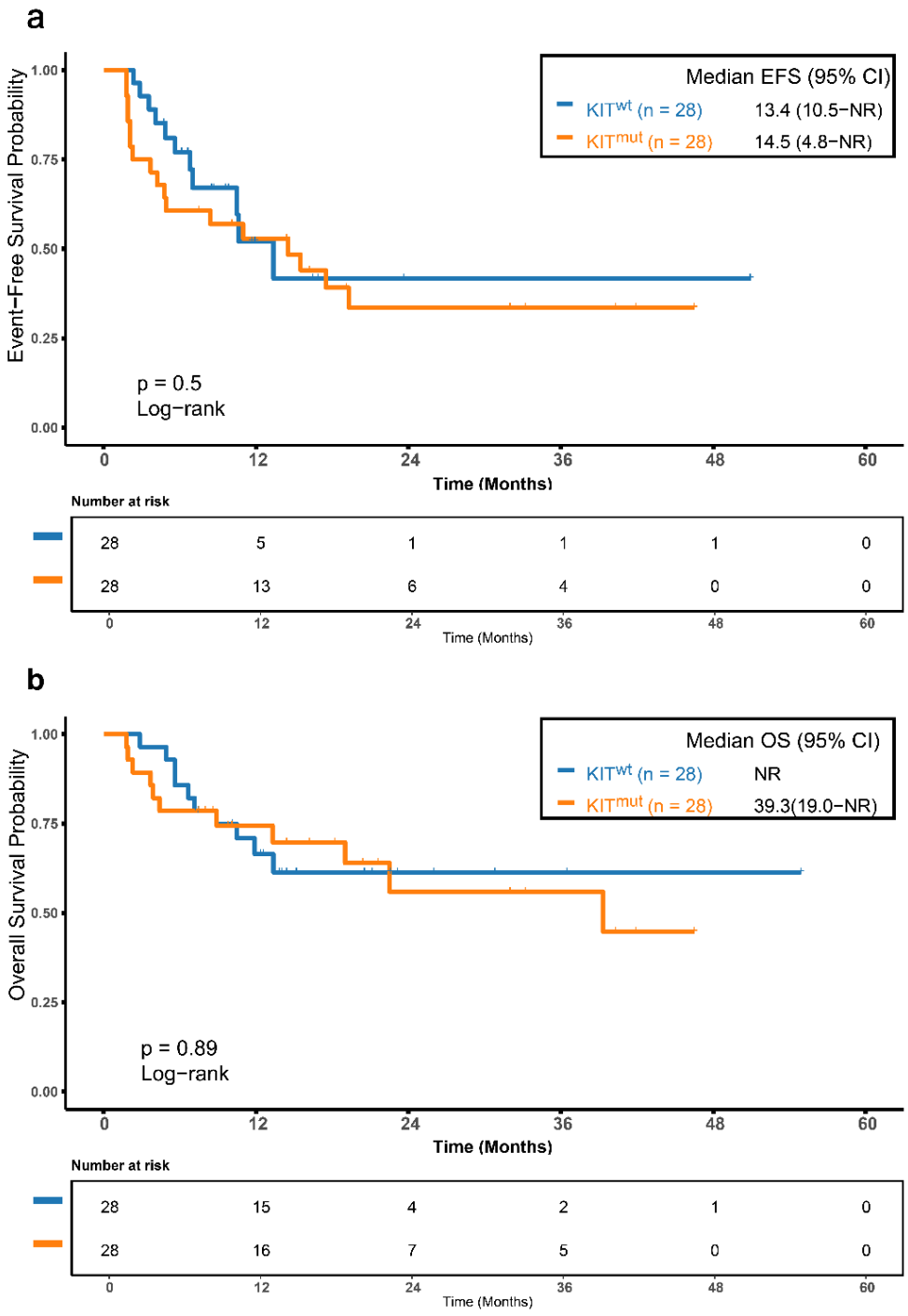


After PSM (12 pairs), the intensive chemotherapy cohort maintained numerical advantages in median EFS (11.0 vs 3.0 months, p=0.36) and median OS (not reached vs 11.8 months, p=0.071), although these differences were not statistically significant.

Figure S2. Survival After PSM: KIT-Mutated vs Wild-Type in VA-Treated Patients

(a) EFS in the matched cohorts.

(b) OS in the matched cohorts.

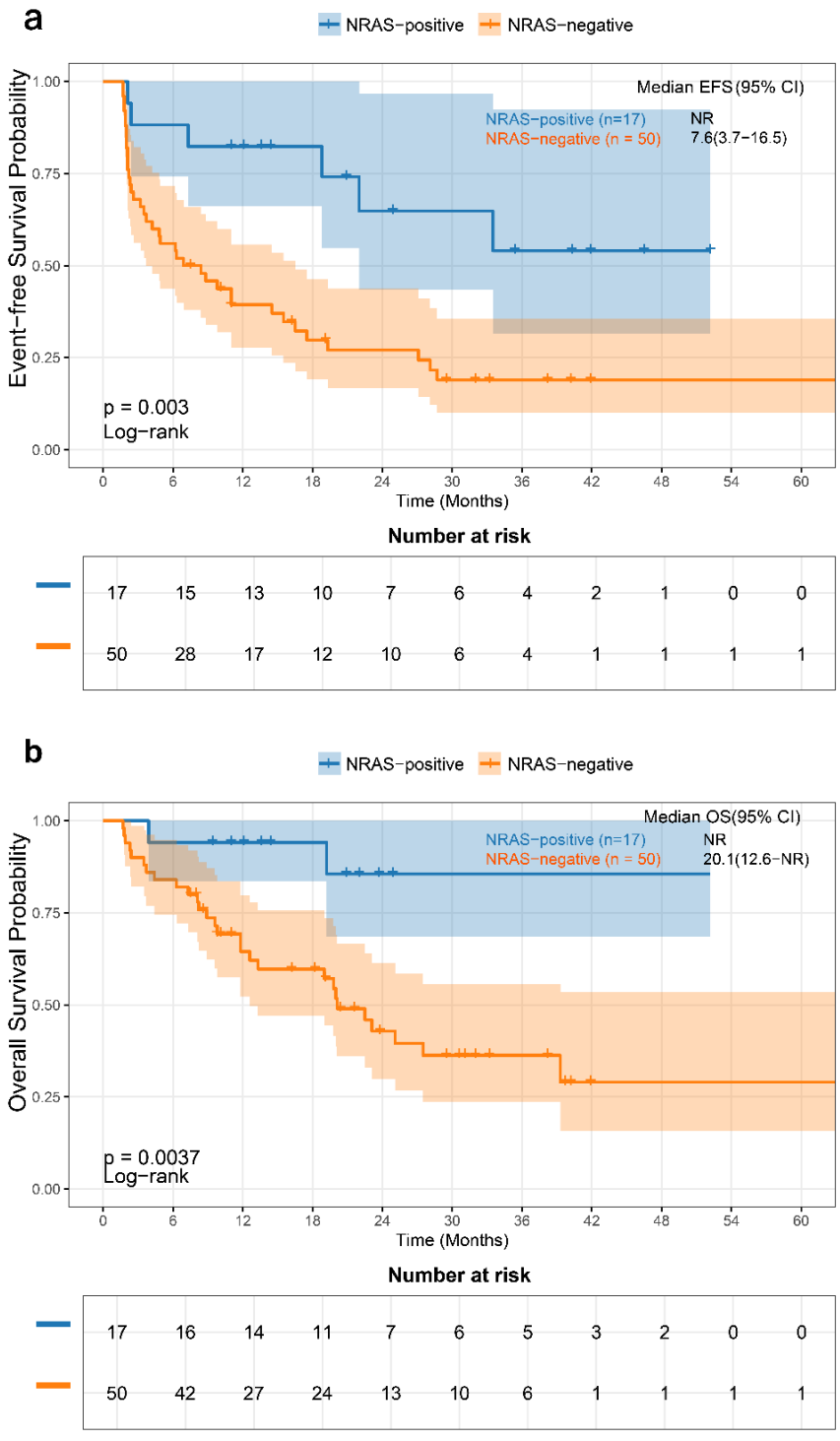


After PSM (28 pairs), differences in EFS (14.5 vs 13.4 months, p=0.5) and OS (39.3 months vs not reached, p=0.89) between KIT-mutated and wild-type patients were no longer statistically significant.

Figure S3. Impact of NRAS Co-mutations in KIT-Mutated AML

(a) EFS by NRAS mutation status.

(b) OS by NRAS mutation status.

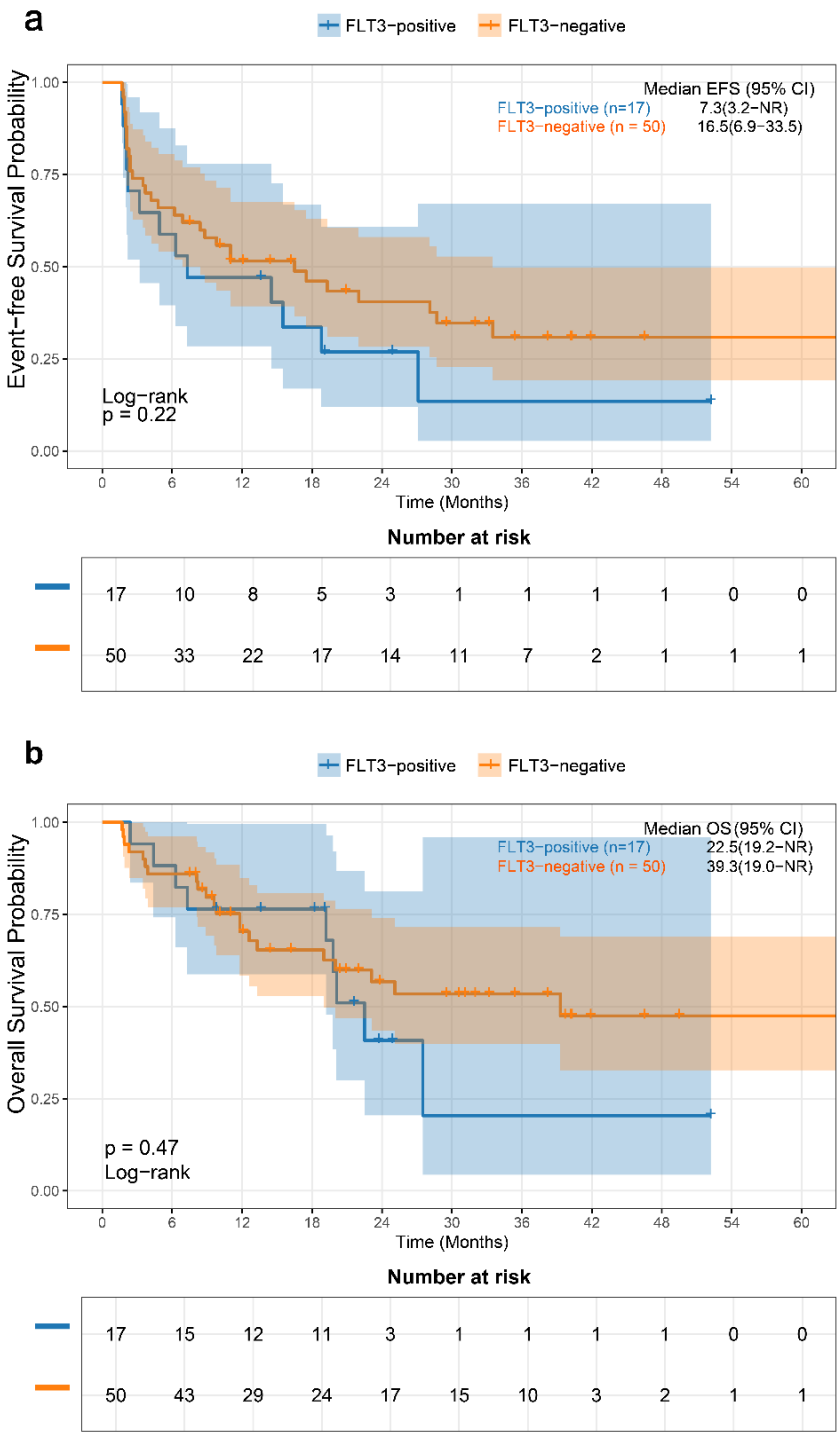


KIT-mutated patients with concurrent NRAS mutations had significantly longer EFS (not reached vs 7.6 months, p=0.003) and OS (not reached vs 20.1 months, p=0.0037) compared to NRAS wild-type patients.

Figure S4. Impact of FLT3-ITD/TKD Co-mutations in KIT-Mutated AML

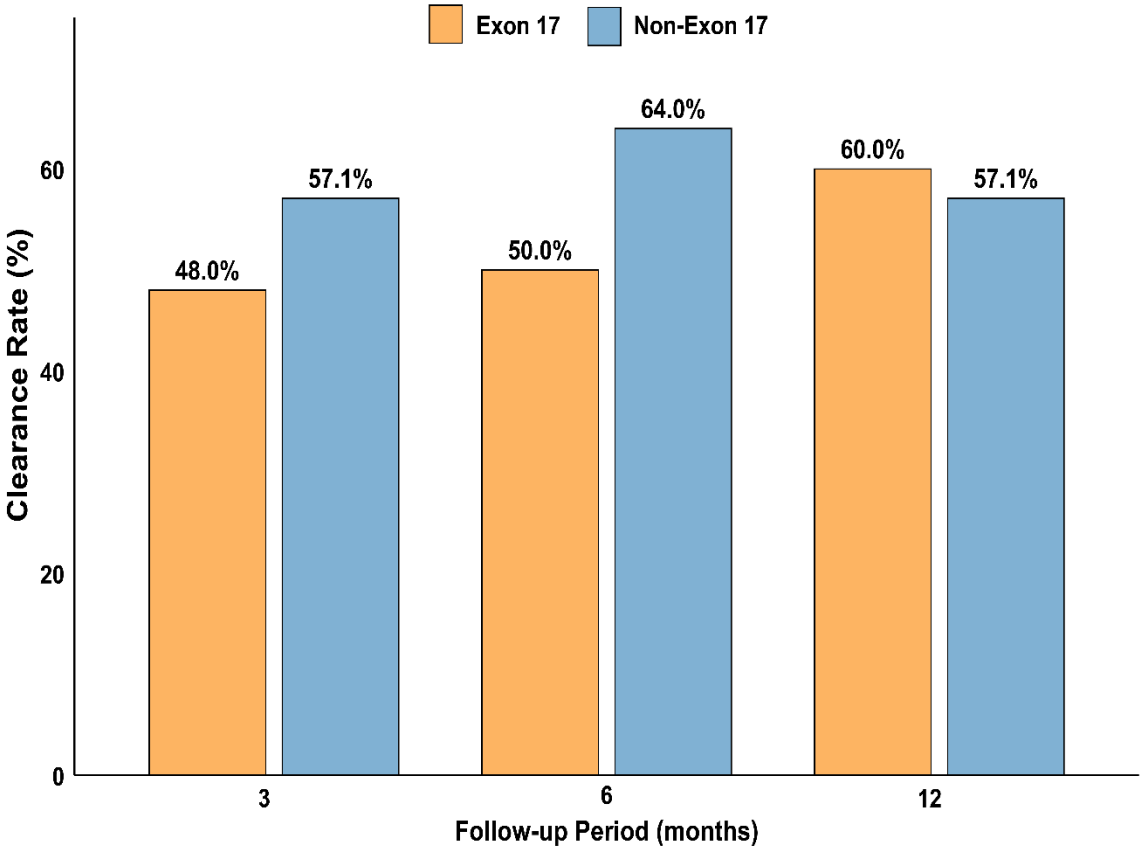
(a) EFS by FLT3-ITD/TKD mutation status.

(b) OS by FLT3-ITD/TKD mutation status.



KIT-mutated patients with FLT3-ITD/TKD mutations showed a trend toward inferior median EFS (7.3 vs 16.5 months, p=0.22) and median OS (22.5 vs 39.3 months, p=0.47) compared to FLT3 wild-type patients, though these differences were not statistically significant.

Figure S5. KIT Mutation Clearance Rates at 3, 6, and 12 Months by Mutation Subgroup



Bar graph comparing the rates of KIT mutation clearance, as assessed by next-generation sequencing, in patients with exon 17 mutations versus non-exon 17 mutations at 3, 6, and 12 months after treatment initiation