Impact of FMS-like tyrosine kinase 3 inhibitor maintenance on post-transplant outcomes in acute myeloid leukemia with FMS-like tyrosine kinase 3 mutations: a real-world German registry analysis highlighting sorafenib

Radwan Massoud,[1] Sarah Flossdorf,[2,3] Franziska Hanke,[2] Thomas Schroeder,[4] Wolfgang Bethge,[5] Robert Zeiser,[6] Caroline Pabst,[7] Gerald Wulf,[8] Elisa Sala,[9] Inken Hilgendorf,[10] Christof Scheid,[11] Matthias Edinger,[12] Friedrich Stölzel,[13] Igor Wolfgang Blau,[14] Matthias Stelljes,[15] Guido Kobbe,[16] Uwe Platzbecker,[17] Jörg Thomas Bittenbring,[18] Matthias Eder,[19] Katharina Fleischhauer,[2,20] Andreas Burchert,[21#] Christoph Schmid[22#] and Nicolaus Kröger[1,2#]

[1]Department of Stem Cell Transplantation, University Medical Center Hamburg-Eppendorf, Hamburg; [2]German Registry for Hematopoietic Stem Cell Transplantation and Cell Therapy, DRST, Ulm; [3]Institute for Medical Informatics, Biometry and Epidemiology (IMIBE), University of Duisburg-Essen, Essen; [4]Department of Hematology and Stem Cell Transplantation, West German Cancer Center, University Hospital of Essen, Essen; [5]Department of Internal Medicine II, Hematology, Oncology, Clinical Immunology and Rheumatology, University Hospital Tübingen, Tübingen; [6]Department of Medicine I - Medical Center, Faculty of Medicine, University of Freiburg, Freiburg; [7]Department of Internal Medicine V, Heidelberg University Hospital, Heidelberg; [8]Hematology and Medical Oncology, University Medicine Göttingen, Göttingen; [9]Department of Internal Medicine, Hematology and Oncology, University Hospital Ulm, Ulm; [10]Department of Internal Medicine, Hematology and Oncology, University Hospital Jena, Jena; [11]Department of Internal Medicine, Hematology and Oncology, University Hospital Cologne, Cologne; [12]Department of Internal Medicine, Hematology and Oncology, University Hospital Regensburg, Regensburg; [13]Department of Internal Medicine, Hematology and Oncology, University Hospital Schleswig Holstein (UKSH) Kiel, Kiel; [14]Medical Clinic, Charité University Medicine Berlin, Berlin; [15]Department of Medicine A, University Hospital of Münster, Münster; [16]Department of Hematology, Oncology and Clinical Immunology, University Hospital Düsseldorf, Heinrich Heine University, Medical Faculty, Düsseldorf; [17]Department of Hematology, Oncology and Stem cell Transplantation, University Hospital Leipzig, Leipzig; [18]Department of Internal Medicine, Hematology and Oncology, University Hospital Homburg, Homburg; [19]Hannover Medical School, Hannover; [20]Institute for Experimental Cellular Therapy, Essen University Hospital, Essen; [21]Department of Hematology, Oncology and Immunology University Hospital Marburg, Marburg[22] and Klinikum Augsburg, II Medizinische Klinik, Augsburg, Germany

[#]*AB, CS and NK contributed equally as senior authors.*

Correspondence: N. Kröger
mmkroeger@outlook.de

Received: November 10, 2025.
Accepted: February 25, 2026.
Early view: March 5, 2026.

https://doi.org/10.3324/haematol.2025.300176

©2026 Ferrata Storti Foundation
Published under a CC BY-NC license

Abstract

FLT3-mutation occurs in 25-30% of acute myeloid leukemia (AML) and confers high relapse risk and inferior survival. Allogeneic hematopoietic cell transplantation (allo-HCT) offers curative potential, yet relapse remains a major post-transplant challenge. Maintenance therapy with FLT3 inhibitors (FLT3i) after allo-HCT has emerged as a promising strategy, but real-world evidence remains limited. This study aimed to assess the impact of FLT3i maintenance on transplant outcomes. We analyzed 523 adults with *FLT3*-internal tandem duplications (ITD) AML in first complete remission who underwent allo-HCT between 2011 and 2023 in 13 German transplant centers participating in the national German Registry for Hemato-poi-

etic Stem Cell Transplantation and Cell Therapy registry; 22% received FLT3i maintenance (sorafenib 49%, midostaurin 37%, gilteritinib 5%, unknown 9%). In multivariable analyses, FLT3i maintenance improved overall survival (OS) (hazard ratio [HR]=2.25; 95% confidence interval [CI]: 1.28-3.95; *P*=0.005), relapse-free survival (RFS) (HR=1.72; 95% CI: 1.05-2.81; *P*=0.030), non-relapse mortality (HR=3.62, 95% CI: 1.08-12.11; *P*=0.037), and graft-*versus*-host disease-free, relapse-free survival (GRFS) (HR=1.59; 95% CI: 1.06-2.40; *P*=0.025). The cumulative incidence of relapse did not differ. In univariate analyses (UVA), OS benefits were observed in MRD-positive (HR=2.35; 95% CI: 1.04-5.31; *P*=0.025) and MRD-negative patients (HR=2.64; 95% CI: 1.05-6.68; *P*=0.020. Sorafenib maintenance (N=50) demonstrated superior efficacy with 5-year OS of 85% *versus* 62% (HR=2.979; *P*=0.0045) and RFS of 84% *versus* 55% (HR=2.771; *P*=0.0043) compared to no maintenance. These real-world findings, while limited by the retrospective design and potential selection bias, align with randomized trial data and support the use of FLT3i maintenance as part of post-transplant care for *FLT3*.

Introduction

Mutations in the FMS-like tyrosine kinase 3 (*FLT3*) gene occurs in approximately 25-30% of newly diagnosed acute myeloid leukemia (AML) patients.[1,2] *FLT3* mutations mainly comprise internal tandem duplications (ITD) or tyrosine kinase domain (TKD) point mutations, with *FLT3*-ITD being associated with increased relapse risk and inferior survival outcomes.[3,4]

Historically, the *FLT3*-ITD allelic ratio was considered an important prognostic factor, with higher allelic ratios (typically>0.5) associated with worse outcomes.[5] The 2022 European LeukemiaNet (ELN) guidelines eliminated the *FLT3*-ITD allelic ratio from risk stratification, with all *FLT3*-ITD mutations now classified as intermediate-risk regardless of allelic ratios.[6] Patients with *FLT3*-mutated AML typically achieve complete remission rates comparable to those without the mutation; however, they experience significantly higher relapse rates and shorter overall survival.[7] This unfavorable prognosis has driven the development of FLT3-targeted therapies, several of which are now integrated into standard AML treatment algorithms.[8,9]

Allogeneic hematopoietic stem cell transplantation (allo-HCT) remains the most effective consolidation strategy for eligible patients with *FLT3*-mutated AML in first complete remission (CR1).[7] However, post-transplant relapse remains a major cause of treatment failure.[10,11] Post-transplant FLT3-inhibitor (FLT3i) maintenance has therefore been investigated as a strategy to reduce relapse risk, with prospective trials demonstrating improved outcomes, particularly with sorafenib-based approaches.[12-14] Using the German Registry for Hematopoietic Stem Cell Transplantation and Cell Therapy (DRST), we evaluated the association of post-transplant FLT3i maintenance with survival and relapse-related outcomes in patients with *FLT3*-mutated AML undergoing allo-HCT in CR1.

Methods

Study design and patient population

This multicenter cohort study was conducted on behalf of the DRST. We included adult patients (≥18 years) from 13 participating centers who underwent allo-HCT for *FLT3*-mutated AML in first CR1 between 2011 and 2023. A predefined subgroup analysis assessed outcomes according to post-transplant sorafenib maintenance, stratified by measurable residual disease (MRD) status at transplantation. MRD was assessed locally using multiparameter flow cytometry (MFC) and/or polymerase chain reaction (PCR) for *NPM1* mutations or leukemia-specific fusion transcripts, according to institutional standards. MFC assays typically had sensitivities of 10^{-3}-10^{-4}, and PCR assays approximately 10^{-4}-10^{-5}. MRD negativity was defined as absence of detectable disease by the locally applied assay. Due to the registry design, platforms and thresholds varied between centers; this heterogeneity is acknowledged as a limitation. Initiation of FLT3i maintenance was at the discretion of the treating physician. Decisions reflected patient fitness, graft-*versus*-host disease (GVHD) status, donor type, evolving evidence over time, drug availability and reimbursement. No standardized protocol was implemented across centers. Only patients from centers with complete documentation of FLT3i maintenance status (maintenance *vs*. no maintenance) were included in the analysis.

A detailed list of participating authors, their affiliated centers, and the number of patients contributed is provided in the *Online Supplementary Appendix*.

Endpoints and definitions

Endpoints included, overall survival (OS), relapse-free survival (RFS), non-relapse mortality (NRM), cumulative incidence of relapse (CIR), and GVHD-free, relapse-free survival (GRFS).

To reduce immortal-time bias, all time-to-event analyses used a day +100 landmark design. Patients who relapsed or died before day +100 after allo-HCT were excluded from the analytic cohort, and follow-up for OS, RFS, GRFS, NRM and CIR was measured from day +100 onwards. This landmark was chosen because FLT3i maintenance was typically initiated between days 30 and 90 (median of 65-75 days depending on the FLT3i type), so that most patients who could start maintenance were alive and evaluable at the time origin. Patients were censored at the last follow-up if

Table 1. Patients donor and transplant characteristics.

Variable	Total, N (%)	Yes, N (%)	No, N (%)
Age, years			
Median (range)	54 (18-77)	53 (18-70)	55 (20-77)
Sex			
Female	276 (53)	64 (55)	212 (52)
Male	247 (47)	52 (45)	195 (48)
ECOG			
0	354 (68)	79 (68)	275 (68)
1	137 (26)	35 (30)	102 (25)
2	8 (2)	0 (0)	8 (2)
3	1 (0)	0 (0)	1 (0)
Unknown	23 (4)	2 (2)	21 (5)
HCT-CI			
0	236 (45)	61 (53)	175 (43)
2	28 (5)	2 (2)	26 (6)
3	35 (7)	8 (7)	27 (7)
4	8 (2)	2 (2)	6 (1)
5	18 (3)	3 (3)	15 (4)
6	6 (1)	3 (3)	3 (1)
7	2 (0)	1 (1)	1 (0)
8	2 (0)	0 (0)	2 (0)
10	1 (0)	0 (0)	1 (0)
Unknown	187 (36)	36 (31)	151 (37)
HCT-CI - 0 if unknown			
0	288 (55)	72 (62)	216 (53)
1	52 (10)	10 (9)	42 (10)
2	54 (10)	7 (6)	47 (12)
3	69 (13)	14 (12)	55 (14)
4	20 (4)	5 (4)	15 (4)
5	23 (4)	3 (3)	20 (5)
6	10 (2)	4 (3)	6 (1)
7	4 (1)	1 (1)	3 (1)
8	2 (0)	0 (0)	2 (0)
10	1 (0)	0 (0)	1 (0)
Graft source			
Bone marrow	25 (5)	7 (6)	18 (4)
Cord blood	2 (0)	2 (2)	0 (0)
Peripheral blood	496 (95)	107 (92)	389 (96)
Type of allo-HCT			
MMRD	36 (7)	2 (2)	34 (8)
MMUD	53 (10)	8 (7)	45 (11)
MRD	133 (25)	32 (28)	101 (25)
MUD	153 (29)	42 (36)	111 (27)
UD	148 (28)	32 (28)	116 (29)
Conditioning Intensity			
RIC	191 (37)	27 (23)	164 (40)
Unknown	17 (3)	7 (6)	10 (2)
MAC	315 (60)	82 (71)	233 (57)
MRD at Tx			
Negative	203 (39)	49 (42)	154 (38)
Positive	166 (32)	47 (41)	119 (29)
Unknown	154 (29)	20 (17)	134 (33)
MRD 1 year post allo-HCT			
Negative	263 (50)	83 (72)	180 (44)
Positive	46 (9)	14 (12)	32 (8)
Unknown	214 (41)	19 (16)	195 (48)
ELN risk category			
Adverse	83 (16)	15 (13)	68 (16)
Intermediate	440 (84)	101 (87)	339 (83)

no event occurred. OS was defined as time to death from any cause, and RFS as the time to relapse or death. GRFS was defined as time relapse, grade 2-4 acute GVHD, moderate to severe chronic GVHD, or death. CIR was defined as relapse and NRM as death without prior relapse - treated as competing risks/events, and were analyzed using cumulative incidence functions. OS and RFS were estimated using Kaplan-Meier methods and compared using Cox proportional hazards models.

Univariable analyses (UVA) used Cox proportional hazards models for OS, RFS, and GRFS, and Fine-Gray competing risk models for NRM and CIR; continuous variables were categorized.

Multivariable analyses (MVA) applied Cox models to estimate adjusted-hazard ratios (HR) with 95% confidence intervals (CI), with Fine-Gray regression used for NRM and CIR. A two-sided *P* value <0.05 was considered statistically significant. Analyses were performed using R V4.0 (R-Foundation for Statistical Computing, Vienna, Austria).

Results

Patients donor and transplant characteristics

We identified 927 patients reported to the DRST who underwent allo-HCT for *FLT3*-mutated AML in CR1 between 2011 and 2023. After excluding 404 patients with unknown FLT3i maintenance status, the final cohort comprised 523 patients, including 116 who received FLT3i maintenance, predominantly off-label (49% sorafenib, 37% midostaurin, 5% gilteritinib, 9% unknown), and 407 without maintenance. The median year of allo-HCT was 2019 (range, 2012-2021) in the maintenance group and 2018 (range, 2011-2021) in the no-maintenance group.

At allo-HCT, 39% were MRD-negative, 32% MRD-positive, and 29% had unknown MRD status; 95% received peripheral blood stem cell grafts, and 60% underwent MAC. The median time from diagnosis to transplant was 120 days (range, 37-789). Median time to initiation was 74 days (range, 35-273) for sorafenib, 75 days (range, 29-303) for midostaurin, and 65 days (range, 33-215) for gilteritinib; median duration was 486 days (range, 7-909), 269 days (range, 3-520), and 287 days (range, 33-810), respectively. Patients, donors, and transplant characteristics are summarized in Table 1.

ECOG: Eastern Cooperative Oncology Group performance status; ELN: European LerukemiaNet; HCT-CI: Hematopoietic Cell Transplantation-Comorbidity Index; MMRD: mismatched related donor; MMUD: mismatched unrelated donor; MRD: matched related donor; MUD: matched unrelated donor; UD: unrelated donor (includes MUD and MMUD); RIC: reduced-intensity conditioning; Tx: transplantation; MRD at Tx: minimal residual disease status at the time of transplantation; MRD 1 year after allo-HCT: minimal residual disease status 1 year post-transplantation; MAC: myeloablative conditioning.

Transplant outcomes

Univariable analyses are summarized in Table 2 and MVA are summarized in Table 3

Engraftment

Neutrophil engraftment occurred in 106 patients receiving maintenance therapy, 389 patients without maintenance, and 360 patients with unknown maintenance status. Median time to engraftment was 16 days (range, 7-30) in the maintenance group, 16 days (range, 4-47) in the no-maintenance group, and 17 days (range, 9-56) in patients with unknown maintenance status.

Graft-*versus*-host disease

Overall, 488 patients (53%) developed acute GVHD (grades 1-4), while 249 patients (27%) did not and in 190 patients (21%) the status was unknown. The 1-year cumulative incidence from day 100 of acute GVHD grade 2-4 was 7% (95% CI: 0-13) in the maintenance group and 5% (95% CI: 2-9) in the no-maintenance group (HR=0.84; 95% CI: 0.27-2.65; *P*=0.768). The corresponding 1-year cumulative incidence of acute GVHD grade 3-4 was 5% (95% CI: 0-10) in the maintenance group and 4% (95% CI: 2-7) in the no-maintenance group (HR=0.88, 95% CI: 0.28-2.79; *P*=0.833).

The 5-year cumulative incidence from day 100 of chronic GVHD (all grades) was 39% (95% CI: 28-49) in the maintenance group and 40% (95% CI: 34-46) in the no-maintenance group (HR=0.94; 95% CI: 0.64-1.37; *P*=0.749). For chronic GVHD (moderate/severe), the 5-year cumulative incidence was 21% (95% CI: 12-30) in the maintenance group and 25% (95% CI: 20-30) in the no-maintenance group (HR=1.18; 95% CI: 0.71-1.94; *P*=0.527).

Overall survival and relapse-free survival

The 5-year OS rate for the entire cohort was 65% (95% CI: 61-70) (Figure 1A). Patients receiving maintenance therapy exhibited a significantly higher OS compared to those who did not, with a HR of 2.37 (95% CI: 1.39-4.07; *P*=0.0005) (Figure 1B). Specifically, the 5-year OS was 77% (95% CI: 65-90) in the maintenance group *versus* 62% (95% CI: 56-68) in the no-maintenance group. This difference remained significant over time in MVA, with a HR of 2.25 (95% CI: 1.28-3.95; *P*=0.005) (Table 3).

The 5-year RFS rate for the entire cohort was 60% (95% CI: 56-65) (Figure 1C). Patients receiving maintenance therapy exhibited a significantly higher RFS compared to those who did not, with a HR of 1.81 (95% CI: 1.14-2.89; *P*=0.0073). Specifically, the 5-year RFS was 75% (95% CI: 66-85) in the maintenance group *versus* 55% (95% CI: 48-62) in the no-maintenance group (Figure 1D). This difference remained significant in MVA, with a HR of 1.72 (95% CI: 1.05-2.81; *P*=0.030) (Table 3).

Non-relapse-free mortality and relapse

The cumulative incidence of NRM at 3-years for the entire cohort was 12% (95% CI: 9-15) (Figure 2A). Patients without maintenance had significantly higher NRM than those receiving maintenance (HR=4.42; 95% CI: 1.37-14.26; *P*=0.013), with 5-year NRM rates of 17% (95% CI: 12-22) *versus* 3% (95% CI: 0-7), respectively (Figure 2B). This association remained significant in MVA (HR=3.62; 95% CI: 1.08-12.11; *P*=0.037) (Table 3).

Sixty-five patients relapsed before day 100. The 3-year CIR for the entire cohort was 28% (95% CI: 24-31) (Figure 2A). CIR did not differ between the maintenance and no-maintenance groups (HR=1.25; 95% CI. 0.76-2.08; *P*=0.380), with 5-year CIR rates of 22% (95% CI: 13-31) and 28% (95% CI: 22-34), respectively (Figure 2B). Results were consistent in multivariable analysis (HR=1.30; 95% CI: 0.76-2.23; *P*=0.330) (Table 3).

Graft-*versus*-host disease-free relapse-free survival

The GRFS at 5-years for the entire cohort was 41% (95% CI: 37-46) (Figure 2C). GRFS was significantly higher in the maintenance group (HR=1.45; 95% CI: 1.01-2.08; *P*=0.039) (Figure 2D). Specifically, the 5-year GRFS was 51% (95% CI: 40-66) in the maintenance group *versus* 39% (95% CI: 33-47) in the no-maintenance group. This difference persisted on MVA (HR=1.59; 95% CI: 1.06-2.40; P=0.025) (Table 3).

Subgroup analyses

Measurable residual disease status

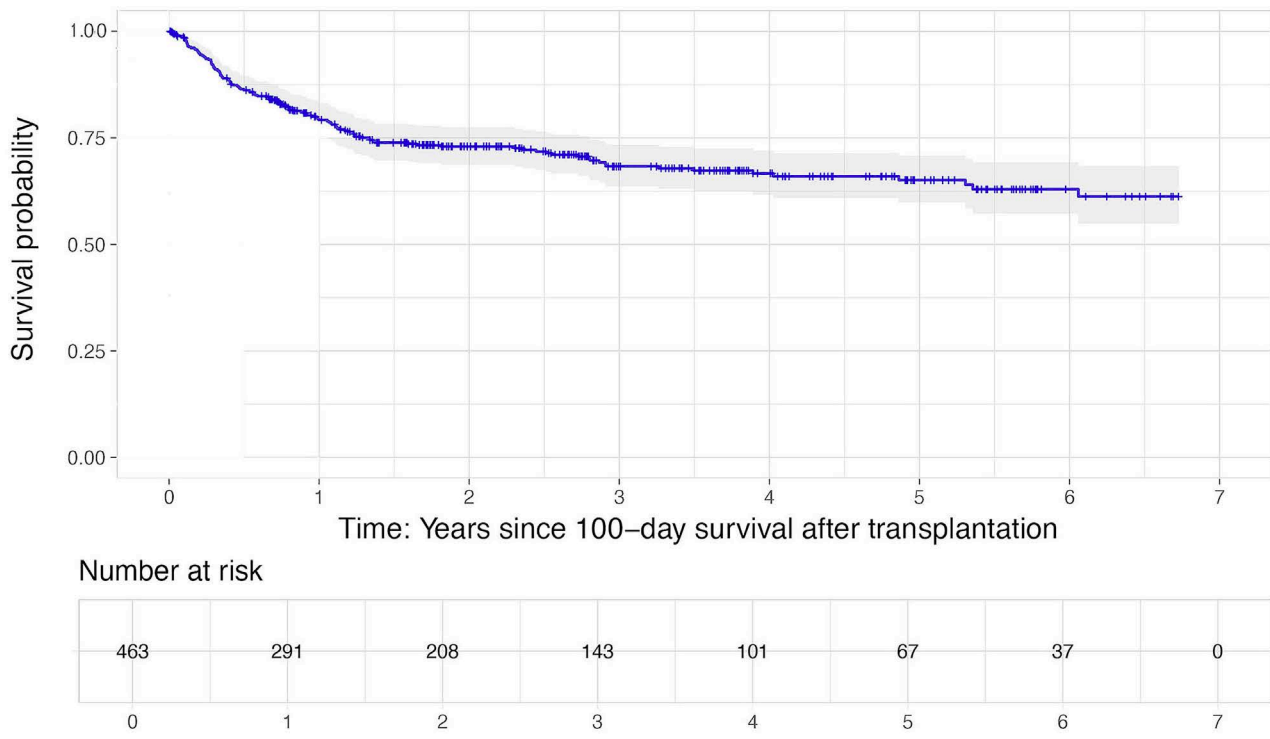
In the subgroup analysis according to MRD status at allo-HCT, MRD-positive patients receiving maintenance showed improved OS (HR=2.35; 95% CI: 1.04-5.31; *P*=0.025), with 5-year OS of 76% (95% CI: 61-94) *versus* 59% (95% CI: 47-73) without maintenance (Figure 3A). RFS at 5-years was higher with maintenance at 72% (95% CI: 58-89) *versus* 55% (95% CI: 43-70) (Figure 3B). NRM and CIR were comparable between groups; NRM HR was 3.19 (95% CI: 0.40-25.26), with 5-year NRM of 3% (95% CI: 0-9) for patient receiving maintenance *versus* 9% (95% CI: 2-15) in the no-maintenance group (Figure 3C). CIR HR was 1.22 (95% CI: 0.57-2.62), with 5-year CIR of 25% (95% CI: 11- 40) with maintenance *versus* 37% (95% CI: 24-50) in the no-maintenance group (Figure 3C). GRFS at 5-years was 43% (95%

Table 2. Univariable analysis.

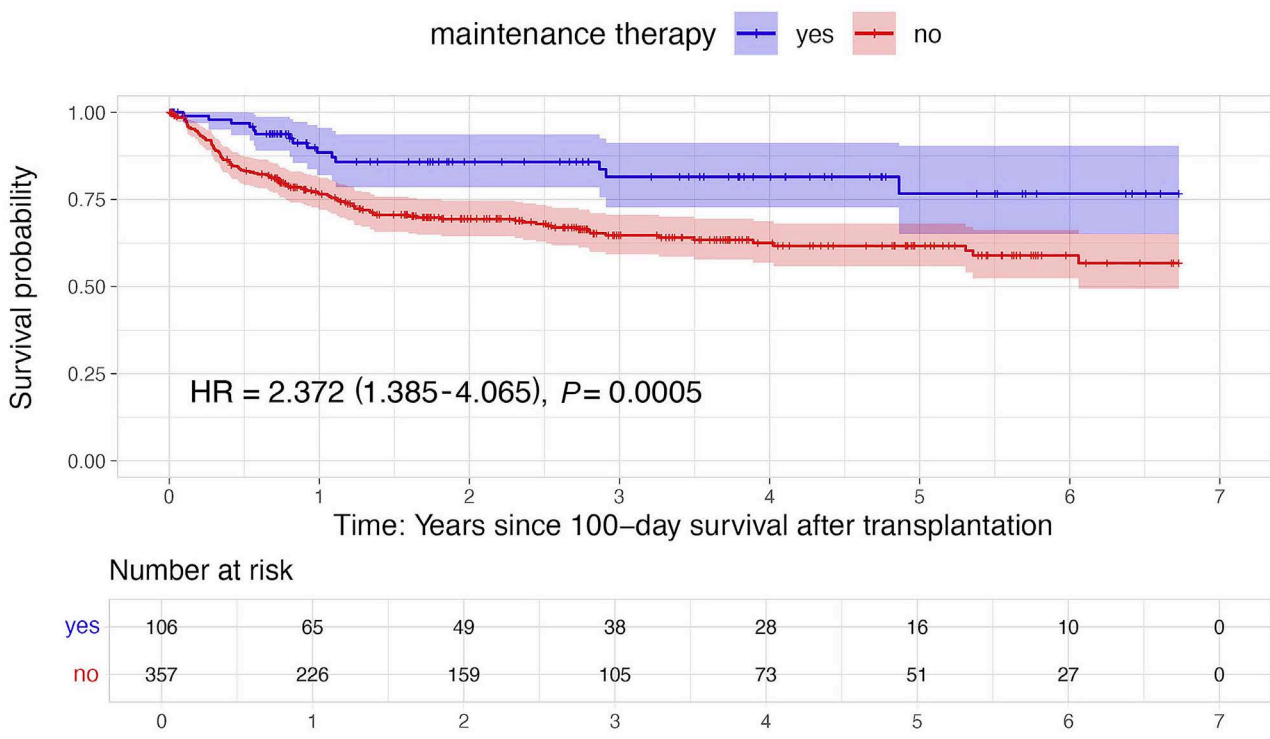
Variable	*HR	95% CI	*P*
OS	2.37	1.39-4.07	0.0005
RFS	1.8	1.14-2.89	0.0073
GRFS	1.45	1.01-2.08	0.039
Relapse	1.25	0.76-2.08	0.38
NRM	4.42	1.37-14.26	0.013

OS: overall survival; RFS: relapse-free survival; GRFS: graft-*versus*-host disease-free, relapse-free survival; NRM: non-relapse mortality; HR: hazard ratio; CI: confidence interval; *HR, 95% CI and *P* refer to the overall follow-up period.

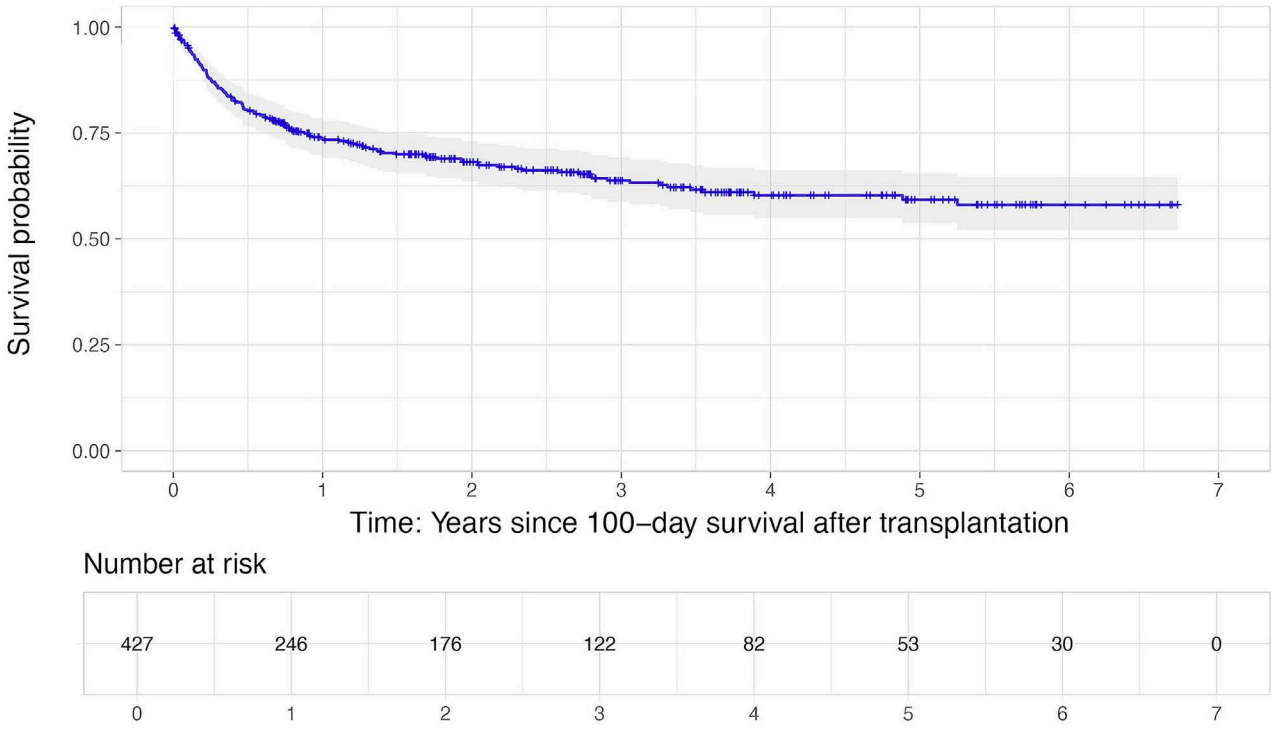
A



B



C



Continued on following page.

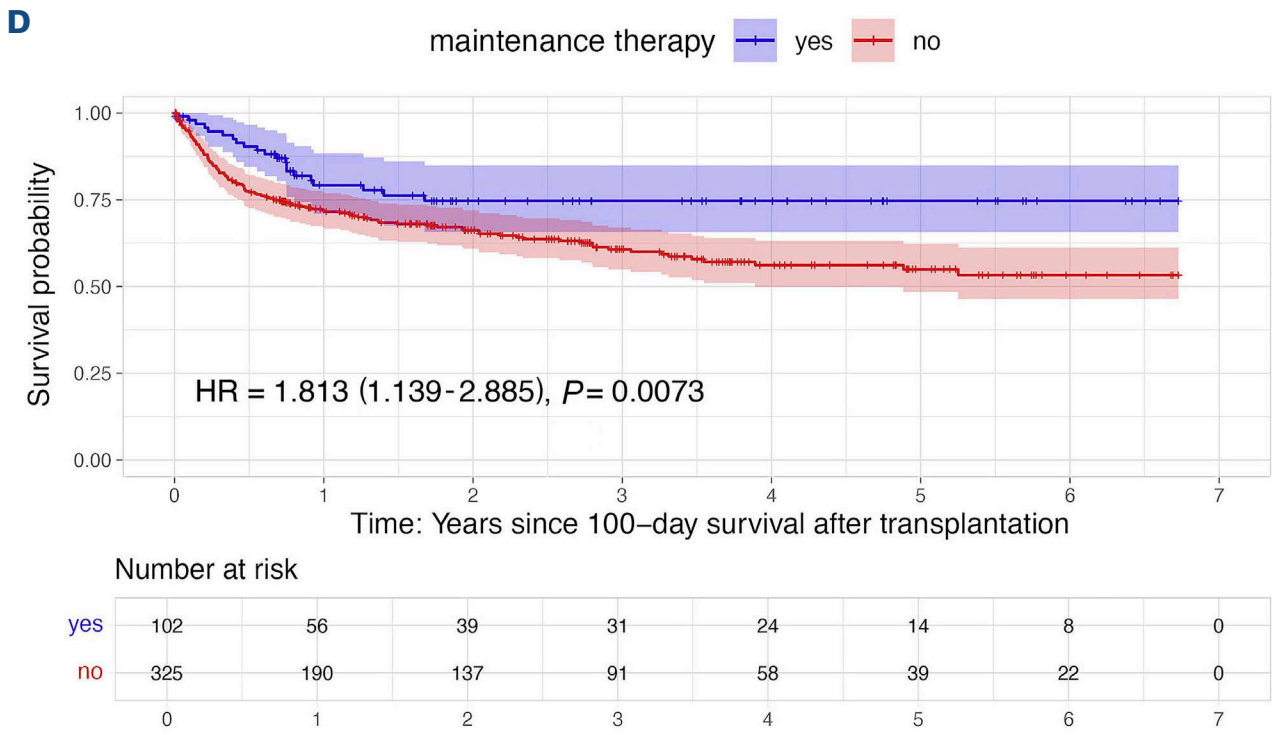


Figure 1. Overall survival and relapse-free survival. (A) Overall survival in the entire cohort. (B) Overall survival, maintenance therapy *versus* no-maintenance therapy. (C) Relapse-free survival in the entire cohort. (D) Relapse-free survival, maintenance therapy *versus* no-maintenance therapy. HR: hazard ratio (95% confidence interval).

CI: 27-66) with maintenance *versus* 31% (95% CI: 20-47) without maintenance (Figure 3D).

Similarly, in MRD-negative patients, maintenance was associated with improved OS (HR=2.64; 95% CI:1.05-6.68; *P*=0.02) and RFS (HR=2.06; 95% CI; 0.97-4.35; *P*=0.04). At 5-years, OS was 86% (95% CI: 75-98) with maintenance *versus* 62% (95% CI: 53-73) without (Figure 4A), and RFS was 78% (95% CI: 65-93) with maintenance *versus* 53% (95% CI: 44-65) without maintenance (Figure 4B). No statistically significant difference in NRM was observed between patients receiving and not receiving maintenance (HR=7.18; 95% CI: 0.95-54.58; *P*=0.057), with 5-year NRM of 3% (95% CI: 0-8) with maintenance *versus* 23% (95% CI: 0-29) (Figure 4C). Although not statistically significant, the point estimate suggests a lower NRM with maintenance. Similarly, no statistically significant difference in CIR was observed between groups (HR=1.18; 95% CI: 0.52-2.66; *P*=0.70), with 5-year CIR rates of 20% (95% CI: 6-33) with maintenance *versus* 24% (95% CI: 15-32) without (Figure 4C). GRFS was also similar between groups (HR=1.59; 95% CI: 0.87-2.90; *P*=0.11), with 5-year GRFS of 58% (95% CI: 41-81) with maintenance *versus* 45% (95% CI: 35-58) without maintenance (Figure 4D).

Exploratory analysis sorafenib versus midostaurin

In the exploratory analysis by FLT3i type, no significant differences were observed when comparing sorafenib versus midostaurin maintenance for any of the transplant outcomes. Results are summarized in the *Online Supplementary Figure S1*.

Sorafenib maintenance analysis (exploratory)

In the overall population, 5-year OS was 85% (95% CI: 73-98) with sorafenib *versus* 62% (95% CI: 56-68) without maintenance (HR=2.98; 95% CI: 1.22-7.30; *P*=0.0045) (Figure 5A). Similarly, 5-year RFS was 84% (95% CI: 73-97) *versus* 55% (95% CI: 48-62) (HR=2.77; 95% CI: 1.22-6.30; *P*=0.0043) (Figure 5B). The 5-year cumulative incidence of relapse was 13% (95% CI: 2-23) in the sorafenib group and 28% (95% CI: 22-34) in the no-maintenance group (HR=1.97; 95% CI: 0.81-4.80; *P*=0.137). Corresponding 5-year NRM was 3% (95% CI: 0-9) *versus* 17% (95% CI: 12-22) (HR=5.65; 95% CI: 0.79-40.67; *P*=0.085) (Figure 5C).

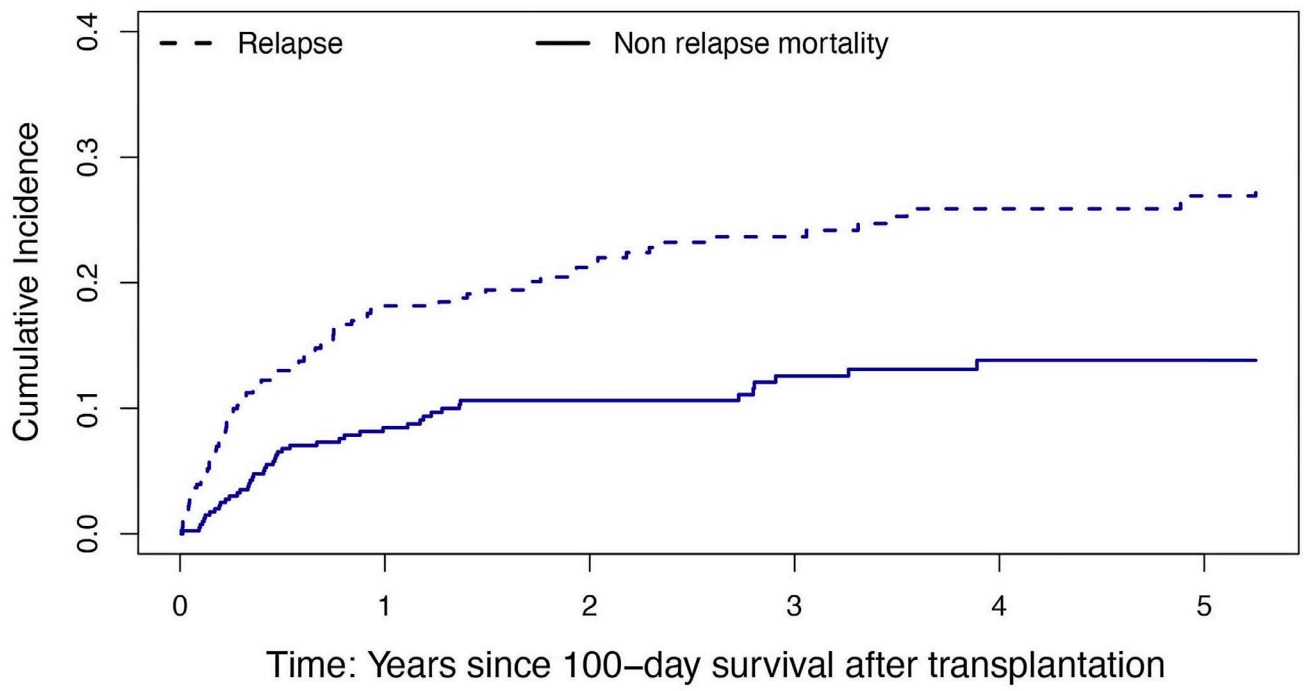
In the exploratory analysis of MRD-positive patients (sorafenib N=24, no maintenance N=138), none of the comparisons reached statistical significance for OS, RFS, CIR, or NRM (*Online Supplementary Figure S2*).

In the exploratory analysis of MRD-negative patients, sorafenib maintenance subgroup analysis (sorafenib N=24 no-maintenance N=138), the 5-year OS was 90% (95% CI: 77-100) in the sorafenib group *versus* 62% (95% CI: 53-73) in the no-maintenance group (HR=3.642; 95% CI: 0.881-15.053; *P*=0.0284) (*Online Supplementary Figure S3A*). The 5-year RFS was 86% (95% CI: 72-100) in the sorafenib group *versus* 53% (95% CI: 44-65) in the no-maintenance group (HR=3.094; 95% CI: 0.963-9.935; *P*=0.0244) (*Online Supplementary Figure S3B*). There were no differences in the 5-year NRM which was 0% in the sorafenib group *versus* 23% CI. 14-32) in the no-maintenance group (NRM analysis not calculable due to zero events in sorafenib group) (*Online Supplementary Figure S3C*).

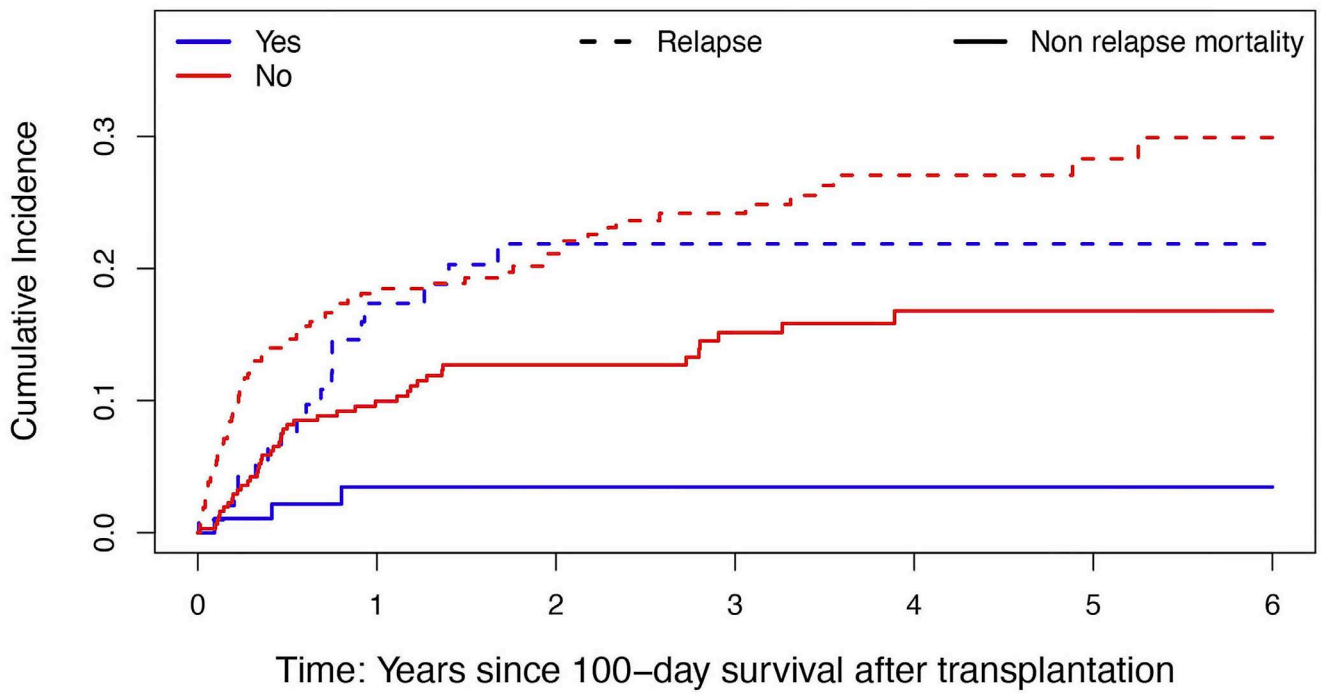
Discussion

Our study of 523 patients with *FLT3*-mutated AML undergoing allo-HCT in CR1 shows that FLT3i maintenance

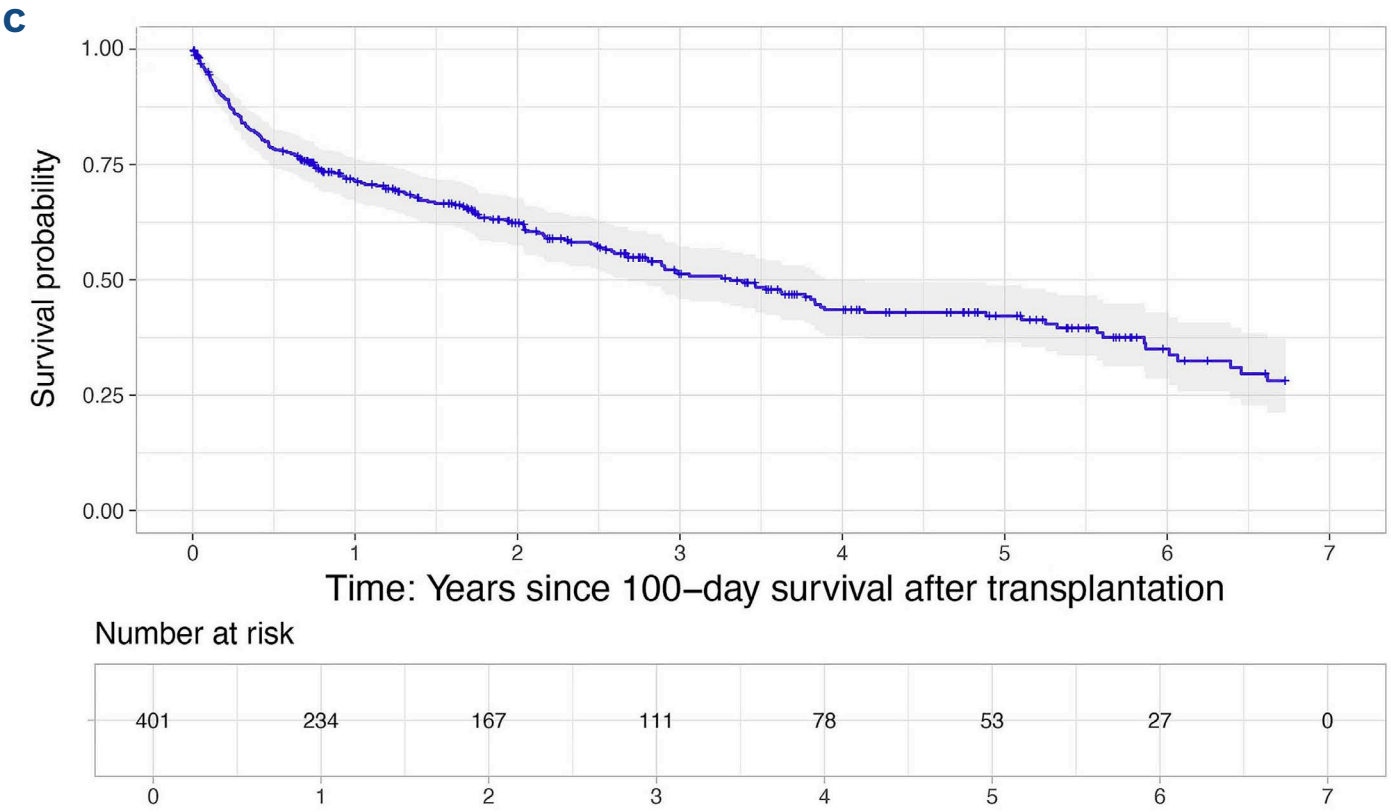
A



B



C



Continued on following page.

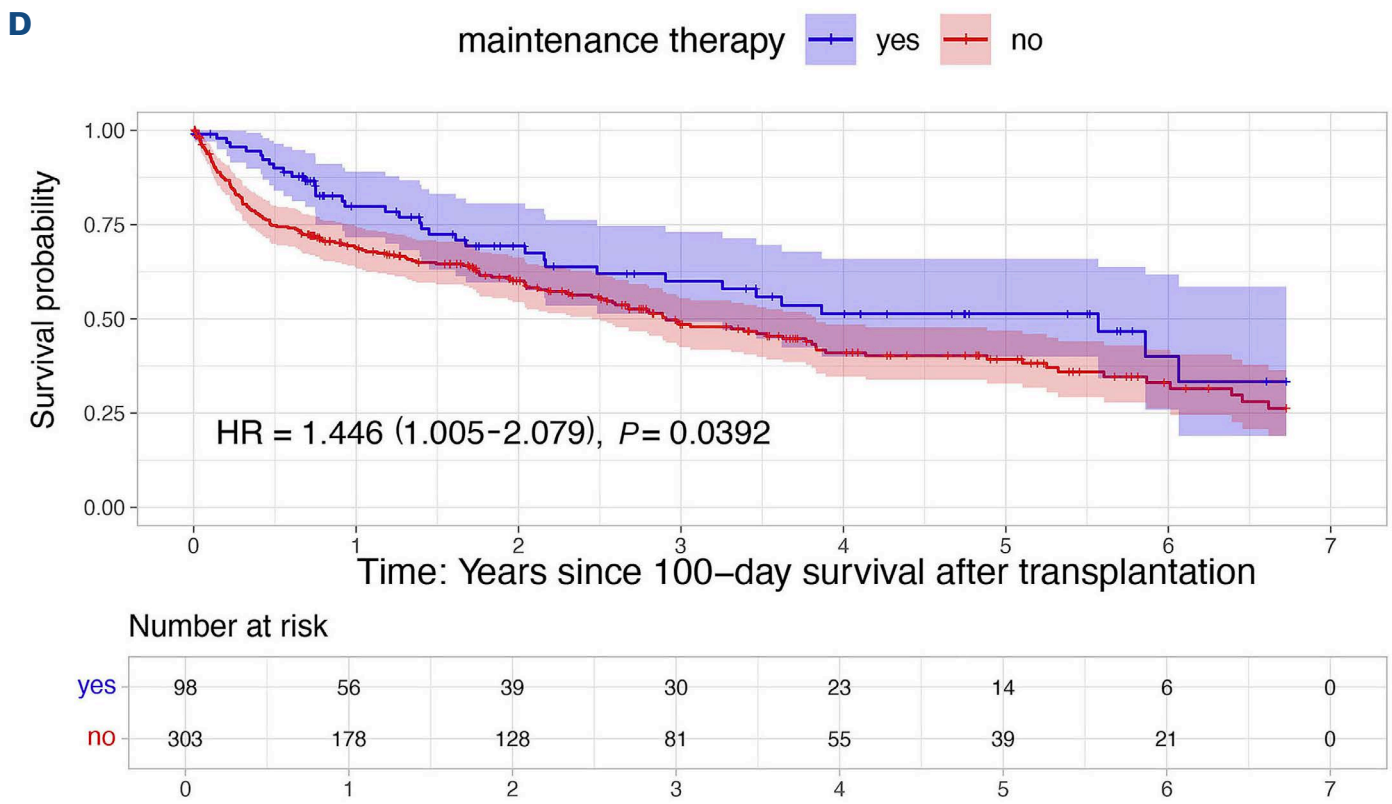


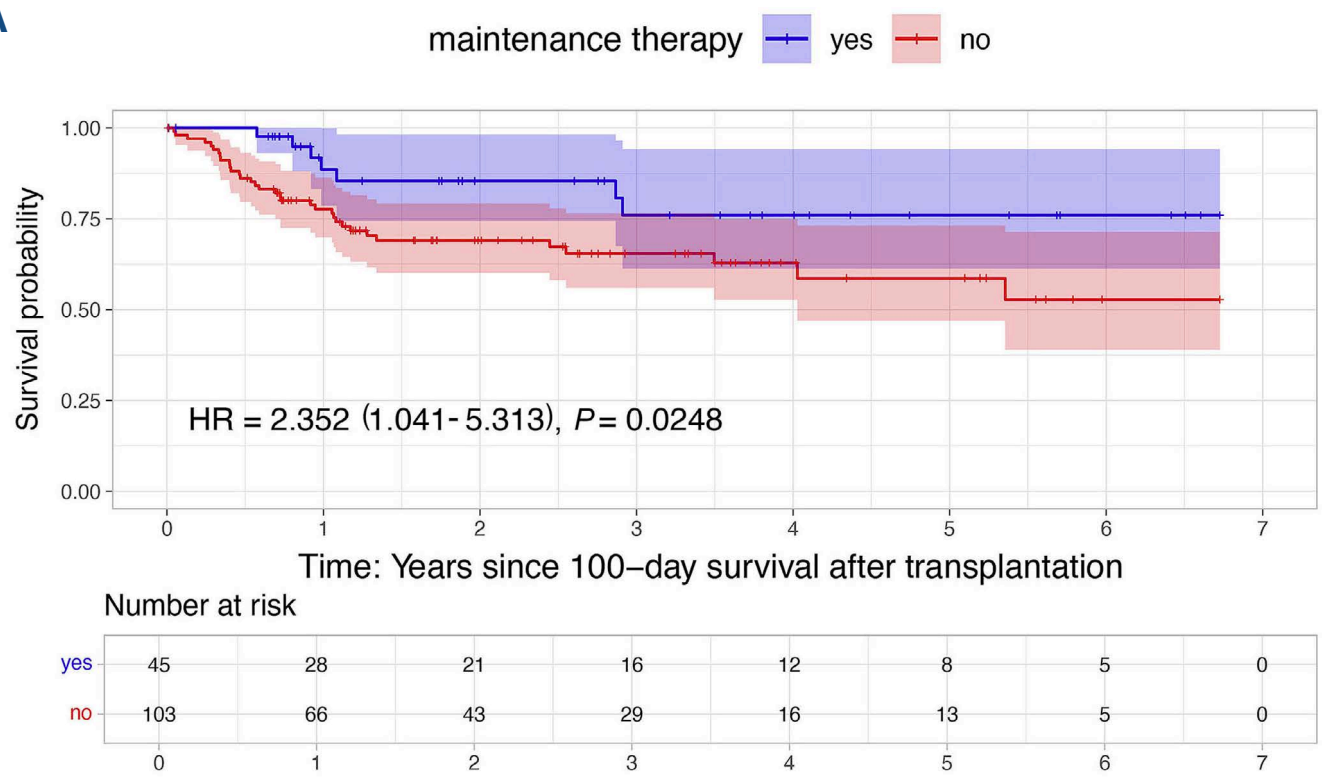
Figure 2. Non-relapse mortality, cumulative incidence of relapse, and graft-*versus*-host disease-free, relapse-free survival. (A) Non-relapse mortality and cumulative incidence of relapse in the entire cohort. (B) Non-relapse mortality and cumulative incidence of relapse, maintenance therapy *versus* no-maintenance therapy. (C) Graft-*versus*-host disease-free, relapse-free survival in the entire cohort. (D) Graft-*versus*-host disease-free, relapse-free survival, maintenance therapy *versus* no-maintenance therapy. HR: hazard ratio (95% confidence interval).

Table3. Multivariable analysis.

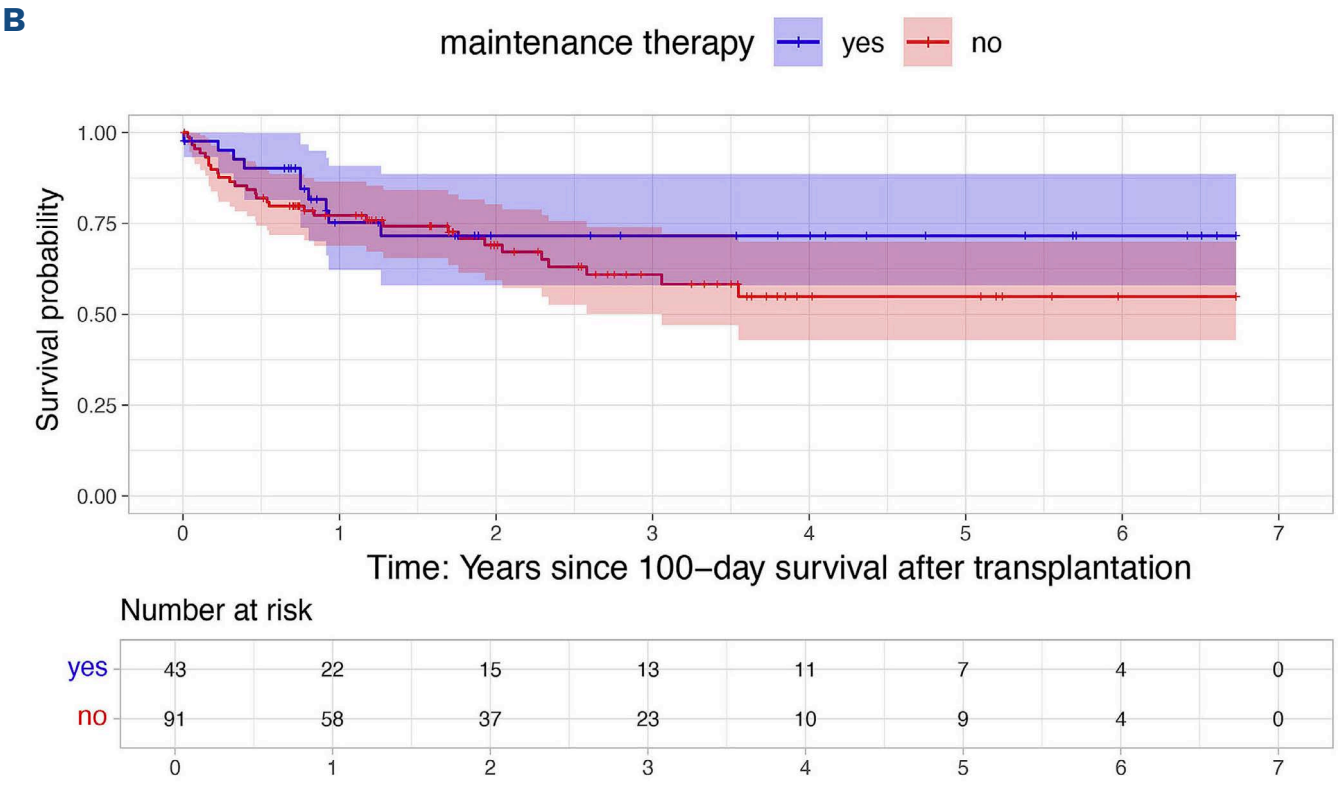
	OS	RFS	GRFS	Relapse	NRM
Variables	**HR (95% CI)** ***P***	**HR (95% CI)** ***P***	**HR (95% CI)** ***P***	**HR (95% CI)** ***P***	**HR (95% CI)** ***P***
N	426	394	372	394	394
Events	119	128	171	87	41
Maintenance therapy: yes *vs.* no	2.25 (1.28-3.95) 0.005	1.72 (1.05-2.81) 0.030	1.59 (1.06-2.40) 0.025	1.30 (0.76-2.23) 0.330	3.62 (1.08-12.11) 0.037
Age, continuous	1.01 (0.99-1.03)	1.00 (0.98-1.01)	1.00 (0.99-1.01)	0.99 (0.97-1.0)	1.02 (0.98-1.06)
Sex: male *vs.* female	1.37 (0.95-1.99)	1.09 (0.76-1.56)	1.00 (0.73-1.37)	0.80 (0.51-1.26)	1.95 (1.00-3.78)
Conditioning: MAC *vs.* non-MAC	0.96 (0.65-1.43)	0.99 (0.67-1.45)	1.01 (0.72-1.43)	0.91 (0.57-1.43)	1.08 (0.53-2.22)
ECOG: >0 *vs.* 0	1.39 (0.94-2.07)	1.30 (0.89-1.90)	1.31 (0.94-1.82)	0.92 (0.57-1.49)	2.20 (1.12-4.33)
MRD at allo-HCT: positive *vs.* negative	1.04 (0.66-1.64)	0.89 (0.58-1.38)	1.07 (0.74-1.55)	1.31 (0.80-2.14)	0.36 (0.14-0.95)
MRD at allo-HCT: unknown *vs.* negative	1.22 (0.78-1.91)	0.99 (0.64-1.52)	1.07 (0.73-1.57)	0.99 (0.57-1.71)	1.03 (0.50-2.11)
Year of allo-HCT: continuous	1.07 (0.99-1.16)	1.04 (0.97-1.12)	1.13 (1.05-1.21)	1.04 (0.96-1.13)	1.00 (0.86-1.15)
Donor type: MUD *vs.* MRD	1.19 (0.72-1.96)	0.97 (0.60-1.58)	1.06 (0.72-1.57)	0.95 (0.54-1.67)	1.08 (0.44-2.64)
Donor type: MMUD *vs.* MUD	1.73 (0.93-3.22)	1.12 (0.58-2.15)	1.07 (0.62-1.85)	0.81 (0.35-1.88)	1.72 (0.51-5.79)
Donor type: MMRD *vs.* MUD	0.80 (0.33-1.93)	0.92 (0.42-2.00)	0.92 (0.49-1.74)	0.97 (0.42-2.27)	0.94 (0.19-4.70)
Donor type: UD *vs.* MUD	1.30 (0.79-2.15)	1.22 (0.76-1.93)	0.75 (0.49-1.16)	1.12 (0.65-1.96)	1.28 (0.53-3.08)
ELN: adverse *vs.* intermediate	0.53 (0.30-0.97)	0.80 (0.48-1.34)	1.05 (0.70-1.58)	1.12 (0.62-2.03)	0.36 (0.11-1.16)

OS: overall survival; RFS: relapse-free survival; GRFS: graft-*versus*-host disease-free, relapse-free survival; NRM: non-relapse mortality; HR: hazard ratio; 95% CI: 95% confidence interval; MAC: myeloablative conditioning; MRD: minimal residual disease; allo-HCT: allogeneic hematopoietic cell transplantation; ECOG: Eastern Cooperative Oncology Group performance status; MUD: matched unrelated donor; MRD: matched related donor; MMUD: mismatched unrelated donor; MMRD: mismatched related donor; UD: unrelated donor (includes MUD and MMUD); ELN: European LeukemiaNet risk classification 2022.

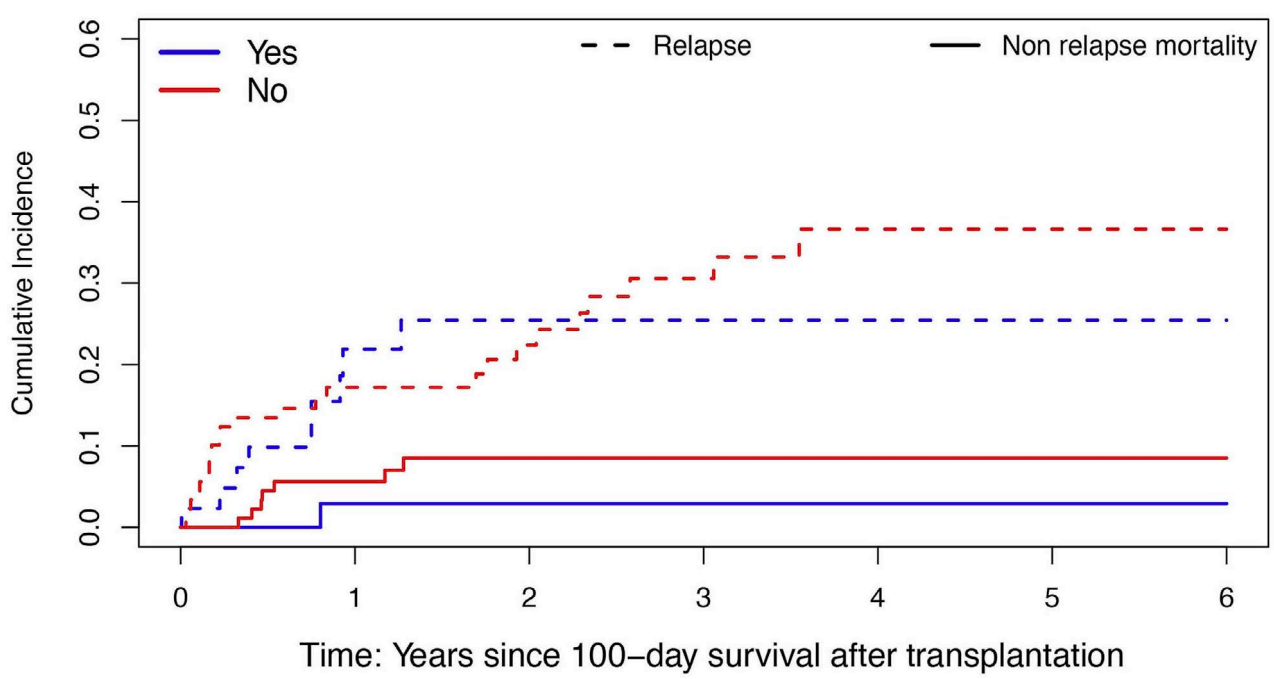
A



B



C



Continued on following page.

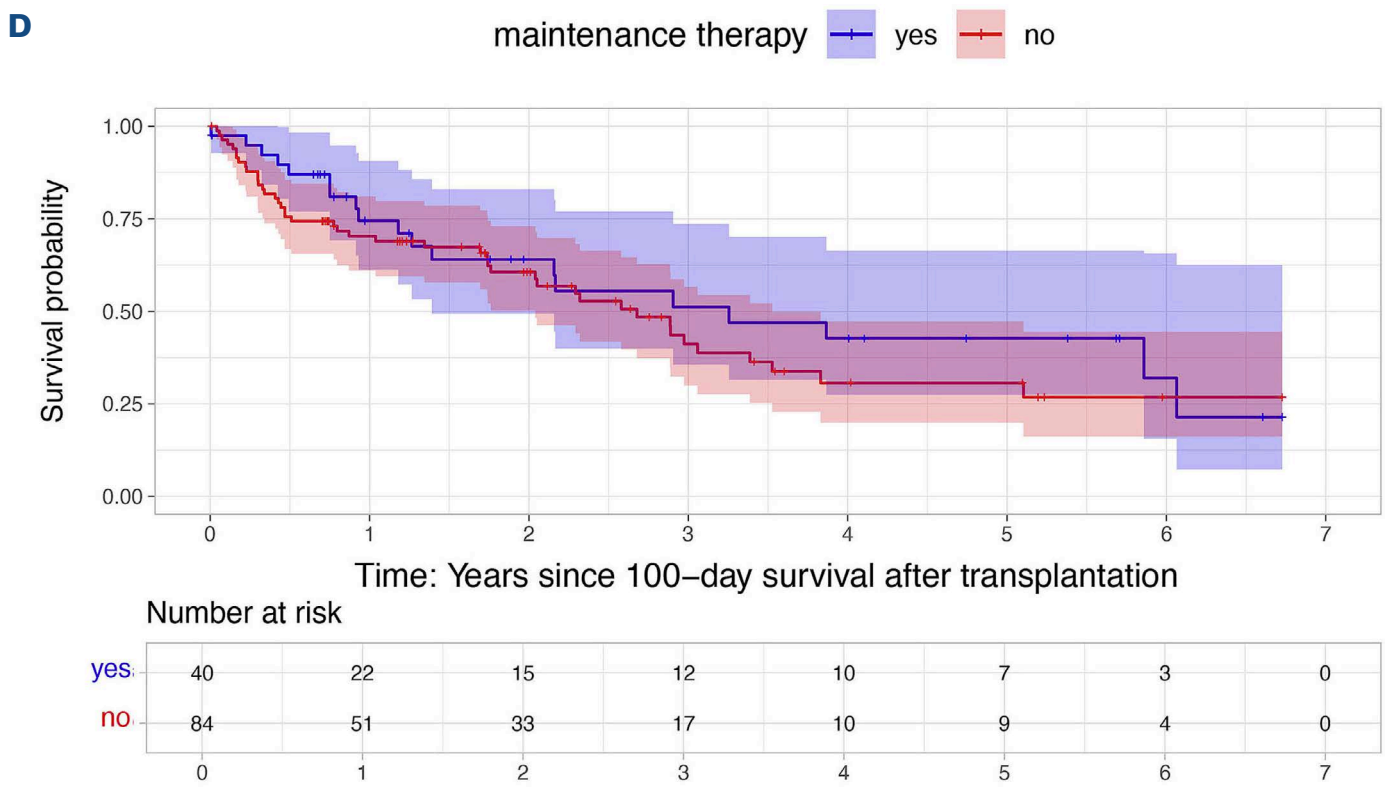


Figure 3. Measurable residual disease-positive subgroup analysis. (A) Overall survival, maintenance therapy *versus* no-maintenance therapy. (B) Relapse-free survival, maintenance therapy *versus* no-maintenance therapy. (C) Non-relapse mortality and cumulative incidence of relapse, maintenance therapy *versus* no-maintenance therapy. (D) Graft-*versus*-host diease-free, relapse-free survival, maintenance therapy *versus* no-maintenance therapy. HR: hazard ratio (95% confidence interval).

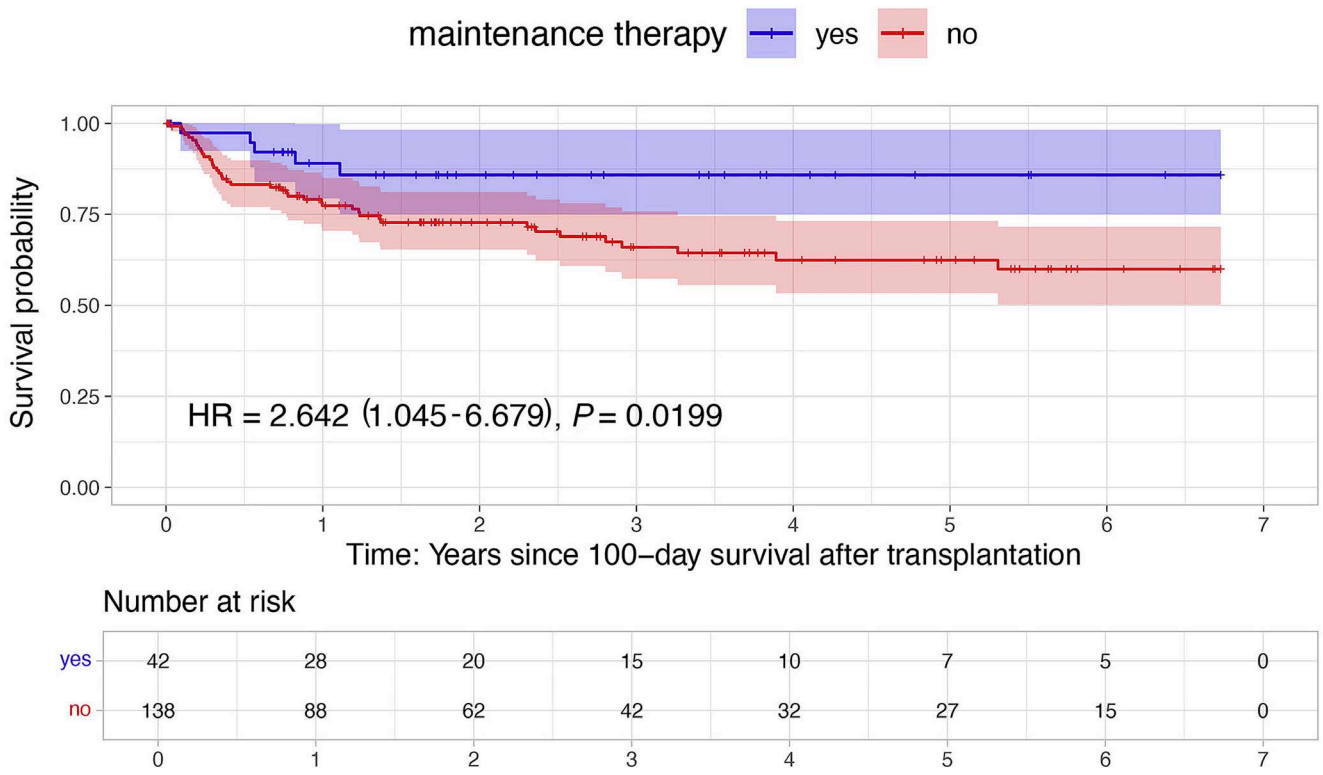
was associated with significantly better post-transplant outcomes in this national real-world cohort. Specifically, FLT3i mantenance was associated with superior OS and RFS, which remained significant on MVA, as well as lower NRM and improved GRFS, while VIR was comparable between the groups.

These findings align closely with prior prospective randomized trials. The SORMAIN trial demonstrated substantial benefits for sorafenib maintenance with significantly lower relapse or death compared to placebo (HR=0.39; *P*=0.013) and marked improvements in RFS at 24 months (85.0% *vs*. 53.3%; *P*=0.002).[12] Similarly, the RADIUS trial reported a trend toward improved outcomes with midostaurin maintenance, although it did not reach statistical significance, highlighting a potential, albeit less pronounced, role for midostaurin compared to sorafenib.[15] Further, the large Chinese multicenter study by Xuan *et al*. reported significantly reduced relapse incidence and improved survival outcomes with sorafenib, reinforcing sorafenib's role as a standard maintenance option.[13] Extended 5-year follow-up data from Xuan *et al*. further confirmed these benefits with higher OS and lower relapse rates.[16] Additionally, the global phase III MORPHO trial evaluating gilteritinib maintenance did not meet its primary endpoint across the entire population but suggested a greater benefit in MRD-positive patients.[14] Smaller phase studies of quizartinib and crenolanib confirmed feasibility and tolerability post-transplant, although definitive efficacy data remain limited.[17, 18]

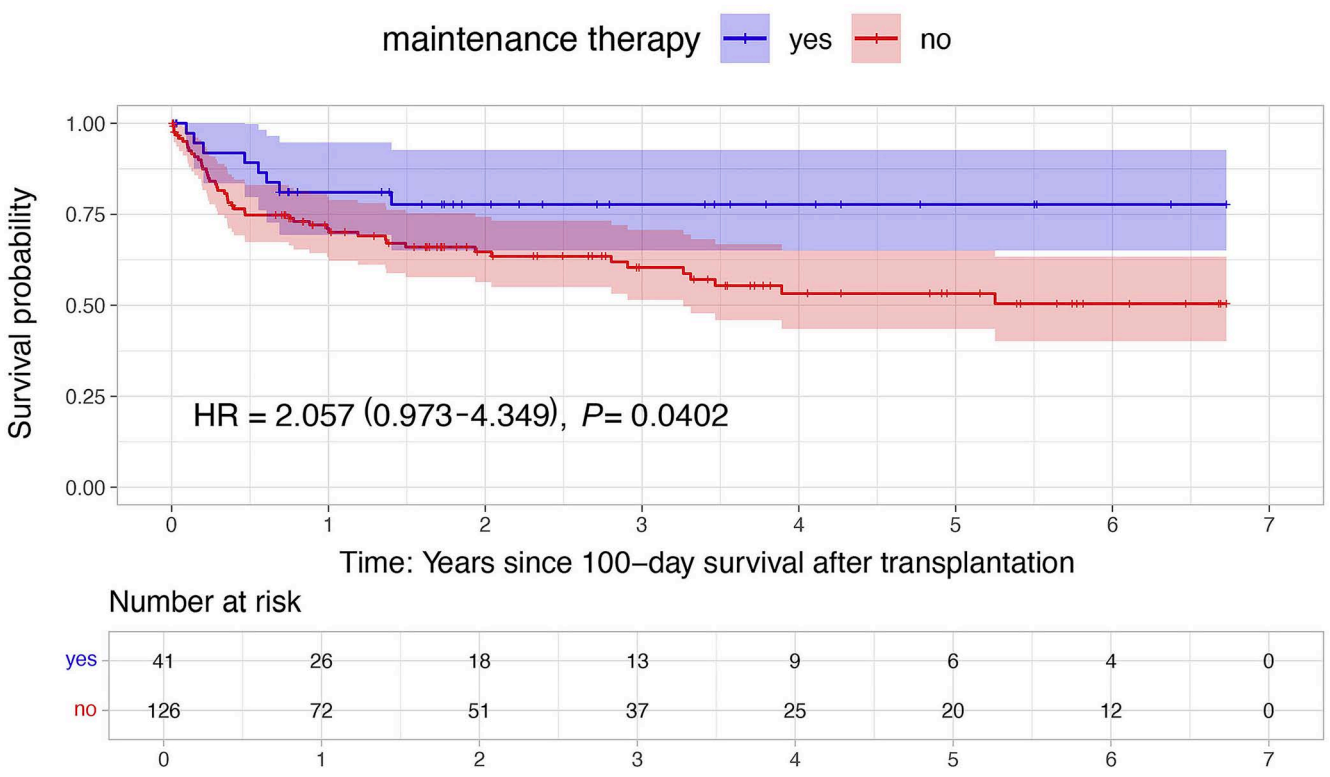
In contrast to randomized trials and meta-analyses where reduced relapse is the principal driver of improved survival with FLT3i maintenance, we observed comparable CIR but substantially lower NRM in the maintenance group. Several factors likely explain this pattern. First, patients receiving maintenance were transplanted more recently, had better performance status, and more often had fully matched donors, introducing residual selection and era effects despite MVA adjustment. Second, the day +100 landmark design excludes early relapse events, which may attenuate detectable differences in CIR while leaving later NRM differences evident. Therefore, the lower NRM observed should be interpreted cautiously and primarily reflects selection rather than a direct therapeutic effect. This interpretation aligns with retrospective studies demonstrating no increase in NRM with FLT3i maintenance.[19-21] Our findings complement smaller retrospective 'real-world' series, including the multicenter study by Shimony *et al*., in which 41 patients received post-transplant sorafenib (N=23) or midostaurin (N=18) and both TKI were feasible and associated with encouraging survival outcomes.[22] Compared with such cohorts, our registry analysis includes a larger number of patients with longer follow-up but is subject to similar limitations in terms of non-standardized indication and residual confounding.

A particularly noteworthy finding in our study is the significant improvement in OS and RFS despite comparable CIR between maintenance and no-maintenance groups. The striking difference in NRM between groups (3% *vs*. 17% at 5 years) appears to be a substantial contributor to the OS advantage. While patient selection factors likely play a role, emerging evidence suggests that FLT3i may enhance immune reconstitution and reduce infection-related mortality post-transplant. Mathew *et al*. demonstrated that

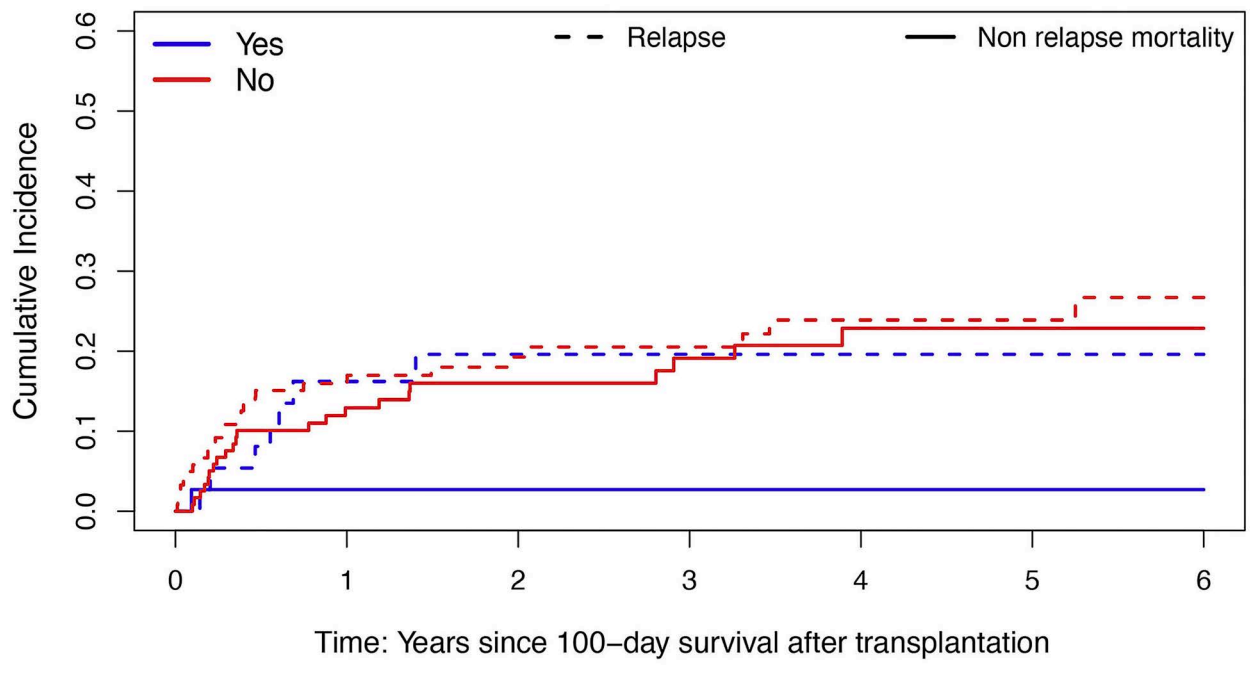
A



B



C



Continued on following page.

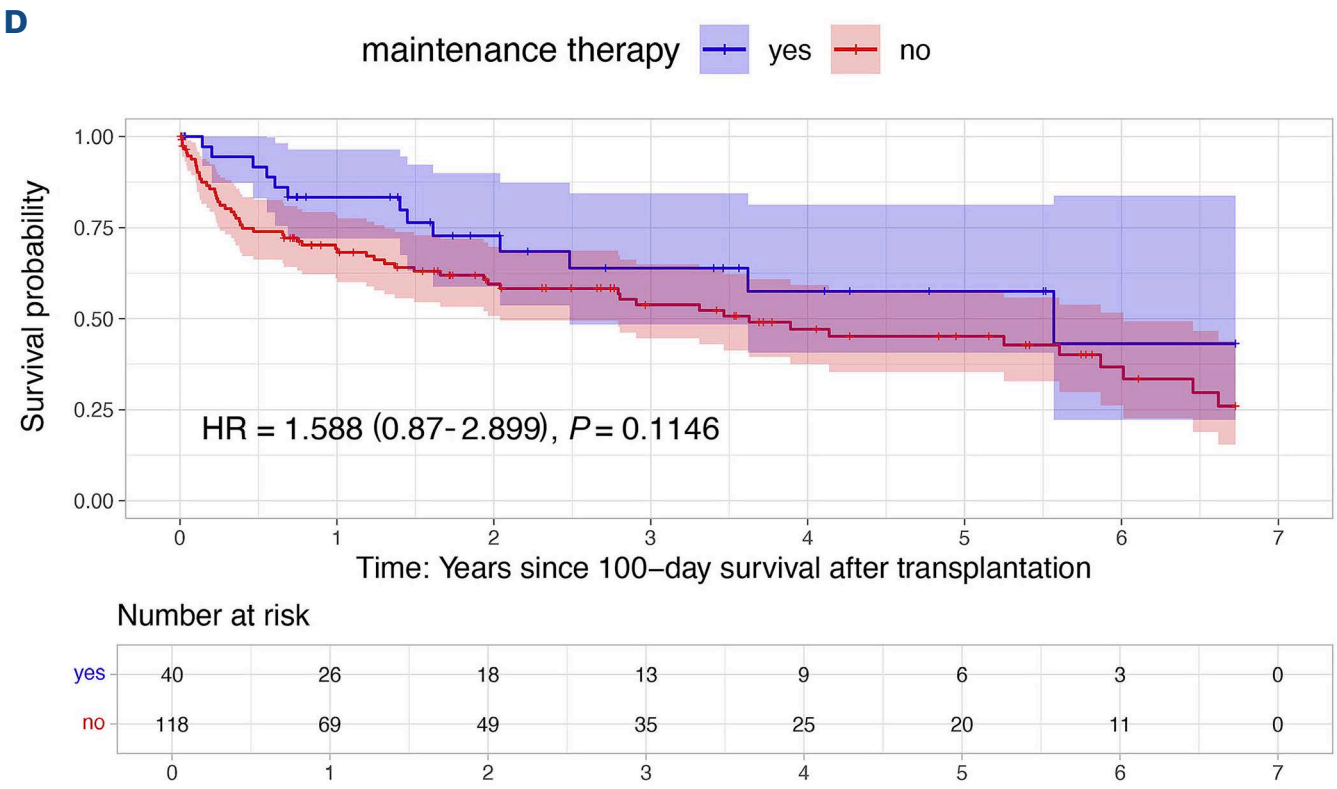


Figure 4. Measurable residual disease-negative subgroup analysis. (A) Overall survival, maintenance therapy *versus* no-maintenance therapy. (B) Relapse-free survival, maintenance therapy *versus* no-maintenance therapy. (C) Non-relapse mortality and cumulative incidence of relapse, maintenance therapy *versus* no-maintenance therapy. (D) Graft-*versus*-host disease-free, relapse-free survival, maintenance therapy *versus* no-maintenance therapy. HR: hazard ratio (95% confidence interval).

sorafenib promotes IL-15 production, enhancing T-cell and NK-cell function, which may improve infection control beyond just anti-leukemic effects.[23] These immunomodulatory benefits could help explain the reduced NRM observed in our maintenance cohort, providing a potential mechanistic explanation for the survival advantage despite comparable relapse rates. However, our registry analyses did not capture infection or cause-specific mortality data. Thus, the lower NRM observed is more likely explained by patient selection and era effects rather than direct protection from infections.

The role of MRD assessment in *FLT3*-mutated AML is particularly relevant in the post-transplant maintenance setting. Recent advances in next-generation sequencing and bioinformatics now enable highly sensitive detection of *FLT3*-ITD for MRD monitoring.[24] Although *FLT3* mutations were historically considered unsuitable MRD markers due to instability and heterogeneity, approximately 70% of FLT3-mutated AML cases harbor co-mutations amenable to MRD monitoring, most commonly NPM1 mutations or fusion genes.[25] Our observation of improved survival in MRD-positive patients receiving FLT3i maintenance is consistent with emerging evidence that FLT3 inhibitors effectively target persistent leukemic clones detected by sensitive MRD assays.[24,26] MRD positivity after induction identifies patients at high relapse risk, and conversion from MRD-negative to MRD-positive status during follow-up strongly predicts inferior outcomes.[26] The MORPHO trial's greater benefit in MRD-positive patients suggests that maintenance therapy is particularly effective against molecularly detectable residual disease.[25,27] This supports routine MRD assessment to guide risk-adapted post-transplant maintenance, including intensified or prolonged therapy for high-risk patients. Future trials should incorporate standardized MRD monitoring to define optimal timing, duration, and FLT3i selection based on dynamic MRD status.[24,25]

Subgroup analyses in our cohort revealed consistent benefits of FLT3i maintenance irrespective of MRD status at transplant, with MRD-positive patients showing especially pronounced survival advantages. This aligns with findings from the MORPHO trial and the SORMAIN trial,[12,14] advocating for the incorporation of MRD assessments in future trials to optimize personalized FLT3i therapy. The SORMAIN trial particularly highlighted significant benefits in MRD-positive patients and suggested benefits, although not statistically significant, in MRD-negative patients.[12] Notably, MRD-negative patients also benefited from maintenance therapy, with 5-year OS of 86% *versus* 62% without maintenance, suggesting persistence of occult residual disease and a preventive effect of maintenance against subsequent relapse.

Our sorafenib subgroup analysis represents the first real-world large cohort study specifically examining sorafenib maintenance therapy after allo-HCT in *FLT3*-ITD AML patients. This analysis of 50 patients receiving sorafenib maintenance *versus* 357 patients without maintenance provides crucial evidence for the clinical efficacy of sorafenib in the post-transplant setting and reveals important insights when compared to both our overall maintenance cohort and existing literature.

In our cohort, sorafenib was the most frequently used FLT3i and showed numerically strong associations with OS and RFS. However, subgroup numbers were limited, particularly

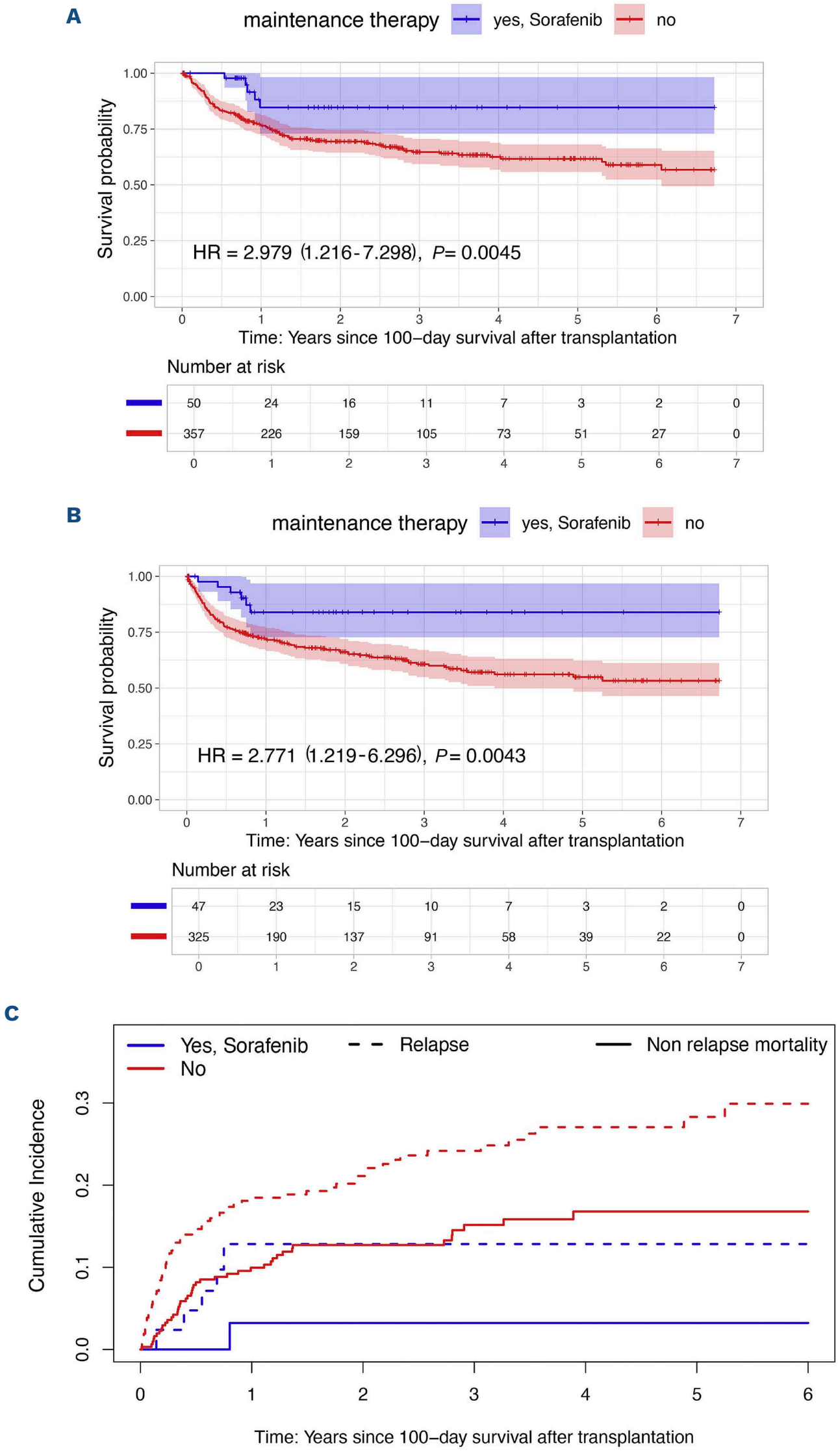


Figure 5. Sorafenib maintenance *versus* no maintenance in the overall population. (A) Overall survival, sorafenib maintenance *versus* no maintenance. (B) Relapse-free survival, sorafenib maintenance *versus* no maintenance. (C) Non-relapse mortality and cumulative incidence of relapse, sorafenib maintenance *versus* no maintenance. HR: hazard ratio (95% confidence interval).

for patients receiving gilteritinib, so these agent-specific findings are exploratory and require confirmation in prospective studies.

Our findings provide important real-world validation of prospective clinical trial results while revealing novel insights. The SORMAIN trial demonstrated substantial benefits for sorafenib maintenance with significantly lower relapse or death compared to placebo (HR=0.39; *P*=0.013) and marked improvements in RFS at 24 months (85.0% *vs*. 53.3%; *P*=0.002).[12] Our analysis confirms the durability of these benefits with 5-year RFS of 84% *versus* 55% (HR=2.771; *P*=0.0043) and 5-year OS of 85% *versus* 62% (HR=2.979; *P*=0.0045), representing the longest follow-up data available for sorafenib maintenance in this population. The large Chinese multicenter study by Xuan *et al*. reported significantly reduced relapse incidence and improved survival outcomes with sorafenib,[13] with extended 5-year follow-up data confirming higher OS and lower relapse rates.[16] Our real-world cohort corroborates these findings with consistent long-term benefits, validating the translation of controlled trial efficacy to routine clinical practice where patient selection, dosing, and duration may vary from protocol specifications.

A particularly important contrast with existing literature emerges from our MRD-stratified analysis. While the SORMAIN trial particularly highlighted significant benefits in MRD-positive patients and suggested non-significant benefits in MRD-negative patients,[12] our study demonstrates the opposite pattern. We observed significant benefits in MRD-negative patients (5-year OS: 90% *vs*. 62%; HR=3.642; *P*=0.0284; RFS: 86% *vs*. 53%; HR=3.094; *P*=0.0244) while MRD-positive patients showed numerical improvements that did not reach statistical significance, likely due to smaller sample size (N=19). This finding suggests that sorafenib maintenance may have broader applicability than previously demonstrated, providing substantial benefit even in patients achieving MRD-negative status post-transplant. The absence of non-relapse mortality events among MRD-negative patients receiving sorafenib may be consistent with previously reported immunomodulatory effects of sorafenib, including IL-15-mediated enhancement of T-cell and NK-cell function,[23] but this observation remains hypothesis-generating and cannot be disentangled from selection and era effects in this registry analysis.

In this registry analysis, the favorable safety profile (5-year NRM 3% *vs*. 17%) and superior outcomes compared with other FLT3i support sorafenib as preferred post-transplant maintenance regardless of MRD status.

Direct comparison of sorafenib and midostaurin showed no differences in OS, RFS, NRM, CIR, or GRFS, likely due to small subgroups. However, when each was compared with no maintenance, sorafenib showed consistently larger effect sizes, suggesting it may be the preferred agent pending larger comparative studies.

The therapeutic landscape for *FLT3*-mutated AML is evolving rapidly with the approval of quizartinib in the pre- and post-transplant setting. In this context, the role of sorafenib maintenance will likely be influenced by prior FLT3i exposure, patterns of resistance and toxicity, and comparative efficacy data. Our real-world findings suggest that sorafenib remains an effective option after allo-HCT, but future prospective studies are needed to determine how best to sequence sorafenib, quizartinib and other FLT3i across the transplant continuum.

Several limitations of our study warrant consideration. First, its retrospective nature introduces potential selection biases, particularly regarding which patients received maintenance therapy. Second, this is a retrospective registry analysis spanning 2011-2023, a period during which indications for allo-HCT, supportive care, and availability of FLT3i changed substantially. Although we adjusted for year of transplant, residual era effects likely remain. In the early part of the study period almost no patients received maintenance, whereas in later years FLT3i became standard in many centers, reinforcing selection and era biases. In addition, physicians were more likely to initiate FLT3i maintenance in patients with hematologic recovery, limited GVHD and preserved organ function, and drug access and reimbursement may have varied between centers and over time. These factors introduce substantial selection bias in favor of the maintenance group and likely contribute to the lower NRM and better survival we observed.

The maintenance cohort was smaller than the no-maintenance group (N=116 *vs*. N=407), limiting subgroup power. Interpretation is further constrained by FLT3i heterogeneity (49% sorafenib, 37% midostaurin, 5% gilteritinib, 9% unknown) and exclusion of 404 patients with unknown maintenance status, which may have introduced selection bias. In addition, *FLT3*-ITD allelic ratio, which may influence benefit from maintenance, was not consistently available in the registry and could therefore not be incorporated into our analyses. Data on treatment at relapse, including subsequent FLT3i use and other targeted therapies, were not systematically collected, so we could not assess how prior maintenance influenced post-relapse management or outcomes.

The clinical implications of our findings are substantial. Our data supports the routine use of FLT3i maintenance after allo-HCT for *FLT3*-mutated AML in CR1, regardless of MRD status at transplant.

Meta-analyses by Fei *et al*. and Gagelmann *et al*. robustly confirm improved OS, RFS, and relapse prevention with FLT3i maintenance post-transplant.[28,29] Retrospective analyses further validate these benefits, consistently showing improved OS, RFS, and reduced relapse without significant increases in NRM or toxicities.[19-21,30-35] Additional retrospective evidence includes single-center studies demonstrating significant DFS and OS improvements upon adjustment for conditioning regimen and donor status,[36] further supporting FLT3i use post-transplant.

Collectively, these comprehensive findings across multiple study designs strongly support FLT3i maintenance as a critical therapeutic strategy to enhance survival outcomes in *FLT3*-mutated AML undergoing allo-HCT.

Future studies should validate MRD-guided maintenance with serial monitoring, define the optimal post-transplant FLT3i, determine maintenance duration using fixed *versus* MRD-adapted strategies, and refine patient selection using biomarkers beyond MRD.

In summary, FLT3i maintenance was associated with improved long-term outcomes in this real-world cohort. However, these results are hypothesis-generating and complement evidence from prospective trials. Sorafenib was the most commonly used agent and showed favorable associations, but agent-specific differences require confirmation in adequately powered studies.

Disclosures

FS has received honoraria from Astellas. MS has served as a consultant for Pfizer, MSD, Bristol-Myers Squibb (BMS), Incyte, Takeda, Astellas, and Amgen; as a speaker for Pfizer, Medac, MSD, Astellas, Jazz Pharmaceuticals, Amgen, Novartis, Kite/Gilead, Celgene, BMS, AbbVie, and Incyte; has received research funding from Pfizer; and has received travel support from Kite/Gilead, Medac, and Pfizer. RZ has served as a consultant for Ironwood Pharmaceuticals, Inc., Neovii, Mallinckrodt, Novartis, and Incyte; has received honoraria from Medac, Sanofi, Mallinckrodt, and Novartis; and has received consultancy or honoraria from Incyte. UP has served as a consultant for Janssen, Amgen, Curis, BMS, AbbVie, Geron, and Novartis; has received honoraria from Janssen and Curis; has received research funding from Janssen, Merck, Amgen, Curis, BMS, AbbVie, and Novartis; has served on advisory boards or boards of directors for BMS and the MDS Foundation; and has received travel support from BMS. NK has received research funding from DKMS; has received speaker honoraria from Alexion and Therakos; has served on advisory boards or boards of directors for BMS, Kite/Gilead, Neovii, Sanofi, and Takeda; and has received speaker honoraria from Kite/Gilead, Neovii, Sanofi, and Takeda. The remaining authors have no conflicts of interest to disclose.

Contributions

RM, NK, AB, and CS designed the study and wrote the manuscript. SF analyzed data and contributed to manuscript writing. All authors interpreted the data, contributed to manuscript writing, and approved the final version of the manuscript.

Acknowledgments

We thank the German Registry for Stem Cell Transplantation and Cell Therapy (DRST) for providing access to registry data used in this study. We are grateful to the participating transplant centers for contributing data and to the staff involved in data collection and curation.

Data-sharing statement

The data supporting the findings of this study are derived from the German Registry for Hematopoietic Stem Cell Transplantation and Cell Therapy (DRST). These data were used under license and are not publicly available. Researchers interested in accessing the data may request them from DRST and/or the corresponding author, subject to approval by the registry.

References

1. Levis M. FLT3 mutations in acute myeloid leukemia: what is the best approach in 2013? Hematology Am Soc Hematol Educ Program. 2013;2013(1):220-226.
2. Daver N, Schlenk RF, Russell NH, Levis MJ. Targeting FLT3 mutations in AML: review of current knowledge and evidence. Leukemia. 2019;33(2):299-312.
3. Kottaridis PD, Gale RE, Frew ME, et al. The presence of a FLT3 internal tandem duplication in patients with acute myeloid leukemia (AML) adds important prognostic information to cytogenetic risk group and response to the first cycle of chemotherapy: analysis of 854 patients from the United Kingdom Medical Research Council AML 10 and 12 trials. Blood. 2001;98(6):1752-1759.
4. Thiede C, Steudel C, Mohr B, et al. Analysis of FLT3-activating mutations in 979 patients with acute myelogenous leukemia: association with FAB subtypes and identification of subgroups with poor prognosis. Blood. 2002;99(12):4326-4335.
5. Dohner H, Estey E, Grimwade D, et al. Diagnosis and management of AML in adults: 2017 ELN recommendations from an international expert panel. Blood. 2017;129(4):424-447.
6. Dohner H, Wei AH, Appelbaum FR, et al. Diagnosis and management of AML in adults: 2022 recommendations from an international expert panel on behalf of the ELN. Blood. 2022;140(12):1345-1377.
7. Schlenk RF, Kayser S, Bullinger L, et al. Differential impact of allelic ratio and insertion site in FLT3-ITD-positive AML with respect to allogeneic transplantation. Blood. 2014;124(23):3441-3449.
8. Stone RM, Mandrekar SJ, Sanford BL, et al. Midostaurin plus chemotherapy for acute myeloid leukemia with a FLT3 mutation. N Engl J Med. 2017;377(5):454-464.
9. Perl AE, Martinelli G, Cortes JE, et al. Gilteritinib or chemotherapy for relapsed or refractory FLT3-mutated AML. N Engl J Med. 2019;381(18):1728-1740.
10. Brunet S, Labopin M, Esteve J, et al. Impact of FLT3 internal tandem duplication on the outcome of related and unrelated hematopoietic transplantation for adult acute myeloid leukemia in first remission: a retrospective analysis. J Clin Oncol. 2012;30(7):735-741.
11. Deol A, Sengsayadeth S, Ahn KW, et al. Does FLT3 mutation impact survival after hematopoietic cell transplant for AML? A CIBMTR analysis. Cancer. 2016;122(19):3005-3014.

12. Burchert A, Bug G, Fritz LV, et al. Sorafenib maintenance after allogeneic hematopoietic stem cell transplantation for acute myeloid leukemia with FLT3-internal tandem duplication mutation (SORMAIN). J Clin Oncol. 2020;38(26):2993-3002.
13. Xuan L, Wang Y, Huang F, et al. Sorafenib maintenance in patients with FLT3-ITD acute myeloid leukaemia undergoing allogeneic haematopoietic stem-cell transplantation: an openlabel, multicentre, randomised phase 3 trial. Lancet Oncol. 2020;21(9):1201-1212.
14. Levis MJ, Hamadani M, Logan B, et al. Gilteritinib as post-transplant maintenance for AML with internal tandem duplication mutation of FLT3. J Clin Oncol. 2024;42(15):1766-1775.
15. Maziarz RT, Levis M, Patnaik MM, et al. Midostaurin after allogeneic stem cell transplant in patients with FLT3-internal tandem duplication-positive acute myeloid leukemia. Bone Marrow Transplant. 2021;56(5):1180-1189.
16. Xuan L, Wang Y, Yang K, et al. Sorafenib maintenance after allogeneic haemopoietic stem-cell transplantation in patients with FLT3-ITD acute myeloid leukaemia: long-term follow-up of an open-label, multicentre, randomised, phase 3 trial. Lancet Haematol. 2023;10(8):e600-e611.
17. Sandmaier BM, Khaled S, Oran B, Gammon G, Trone D, Frankfurt O. Results of a phase 1 study of quizartinib as maintenance therapy in subjects with acute myeloid leukemia in remission following allogeneic hematopoietic stem cell transplant. Am J Hematol. 2018;93(2):222-231.
18. Oran B, Marin D, Bashir Q, et al. Long-term follow-up of crenolanib maintenance after allogeneic transplantation in newly diagnosed and relapsed FLT3 mutated AML. Blood. 2024;144(Suppl 1):1497.
19. Brunner AM, Li S, Fathi AT, et al. Haematopoietic cell transplantation with and without sorafenib maintenance for patients with FLT3-ITD acute myeloid leukaemia in first complete remission. Br J Haematol. 2016;175(3):496-504.
20. Bazarbachi A, Labopin M, Battipaglia G, et al. Allogeneic stem cell transplantation for FLT3-mutated acute myeloid leukemia: in vivo T-cell depletion and posttransplant sorafenib maintenance improve survival. A retrospective Acute Leukemia Working Party-European Society for Blood and Marrow Transplant study. Clin Hematol Int. 2019;1(1):58-74.
21. Chappell G, Geer M, Gatza E, et al. Maintenance sorafenib in FLT3-ITD AML following allogeneic HCT favorably impacts relapse and overall survival. Bone Marrow Transplant. 2019;54(9):1518-1520.
22. Shimony S, Yeshurun M, Wolach O, et al. Post-transplantation maintenance with sorafenib or midostaurin for FLT3 positive AML patients-a multicenter retrospective observational study. Leuk Lymphoma. 2021;62(10):2475-2481.
23. Mathew NR, Baumgartner F, Braun L, et al. Sorafenib promotes graft-versus-leukemia activity in mice and humans through IL-15 production in FLT3-ITD-mutant leukemia cells. Nat Med. 2018;24(3):282-291.
24. Othman J, Potter N, Mokretar K, et al. FLT3 inhibitors as MRDguided salvage treatment for molecular failure in FLT3 mutated AML. Leukemia. 2023;37(10):2066-2072.
25. Reikvam H, Dillon R. Revisiting the role of measurable residual disease in FLT3 mutated acute myelogenous leukemia. Expert Rev Hematol. 2024;17(4-5):103-106.
26. Rücker FG, Bullinger L, Cocciardi S, et al. Measurable residual disease monitoring in AML with FLT3-ITD treated with intensive chemotherapy plus midostaurin. Blood Adv. 2024;8(23):6067-6080.
27. Levis MJ, Hamadani M, Logan BR, et al. BMT CTN Protocol 1506: a phase 3, trial of gilteritinib, as maintenance therapy after allogeneic hematopoietic stem cell transplantation in patients with FLT3-ITD+ AML. Blood. 2019;134(Suppl 1):4602.
28. Gagelmann N, Wolschke C, Klyuchnikov E, Christopeit M, Ayuk F, Kröger N. TKI maintenance after stem-cell transplantation for FLT3-ITD positive acute myeloid leukemia: a systematic review and meta-analysis. Frontiers Immunol. 2021;12:630429.
29. Fei X, Zhang S, Gu J, Wang J. FLT3 inhibitors as maintenance therapy post allogeneic hematopoietic stem cell transplantation in acute myeloid leukemia patients with FLT3 mutations: a meta-analysis. Cancer Med. 2023;12(6):6877-6888.
30. Battipaglia G, Massoud R, Ahmed SO, et al. Efficacy and feasibility of sorafenib as a maintenance agent after allogeneic hematopoietic stem cell transplantation for Fms-like tyrosine kinase 3 mutated acute myeloid leukemia: an update. Clin Lymphoma Myeloma Leuk. 2019;19(8):506-508.
31. Battipaglia G, Ruggeri A, Massoud R, et al. Efficacy and feasibility of sorafenib as a maintenance agent after allogeneic hematopoietic stem cell transplantation for Fms-like tyrosine kinase 3-mutated acute myeloid leukemia. Cancer. 2017;123(15):2867-2874.
32. Griffin JD, Song Y, Yang H, Freimark J, Shah MV. Post-transplant maintenance therapy in patients with FLT3-mutated acute myeloid leukemia: Real-world treatment patterns and outcomes. Eur J Haematol. 2021;107(5):553-565.
33. Shi J, Cao L, Luo Y, et al. Maintenance sorafenib is superior to prophylactic donor lymphocyte infusion at improving the prognosis of acute myeloid leukemia with FMS-like tyrosine kinase 3 internal tandem duplication after allogeneic hematopoietic stem cell transplantation. Bone Marrow Transplant. 2021;56(1):293-296.
34. Diral E, Furnari G, Bruno A, et al. Sorafenib maintenance in FLT3-ITD mutated AML after allogeneic HCT: a real-world, single-center experience. Front Oncol. 2024;14(1391743.
35. Aydin S, Passera R, Scaldaferri M, et al. Sorafenib maintenance after hematopoietic stem cell transplantation improves outcome of FLT3-ITD-mutated acute myeloid leukemia. Int J Hematol. 2022;116(6):883-891.
36. He G, Belmont E, Karrison T, et al. FLT3 inhibitor maintenance after allogeneic stem cell transplantation in FLT3-mutated acute myeloid leukemia (AML) patients. Ann Transl Med. 2024;12(3):49.