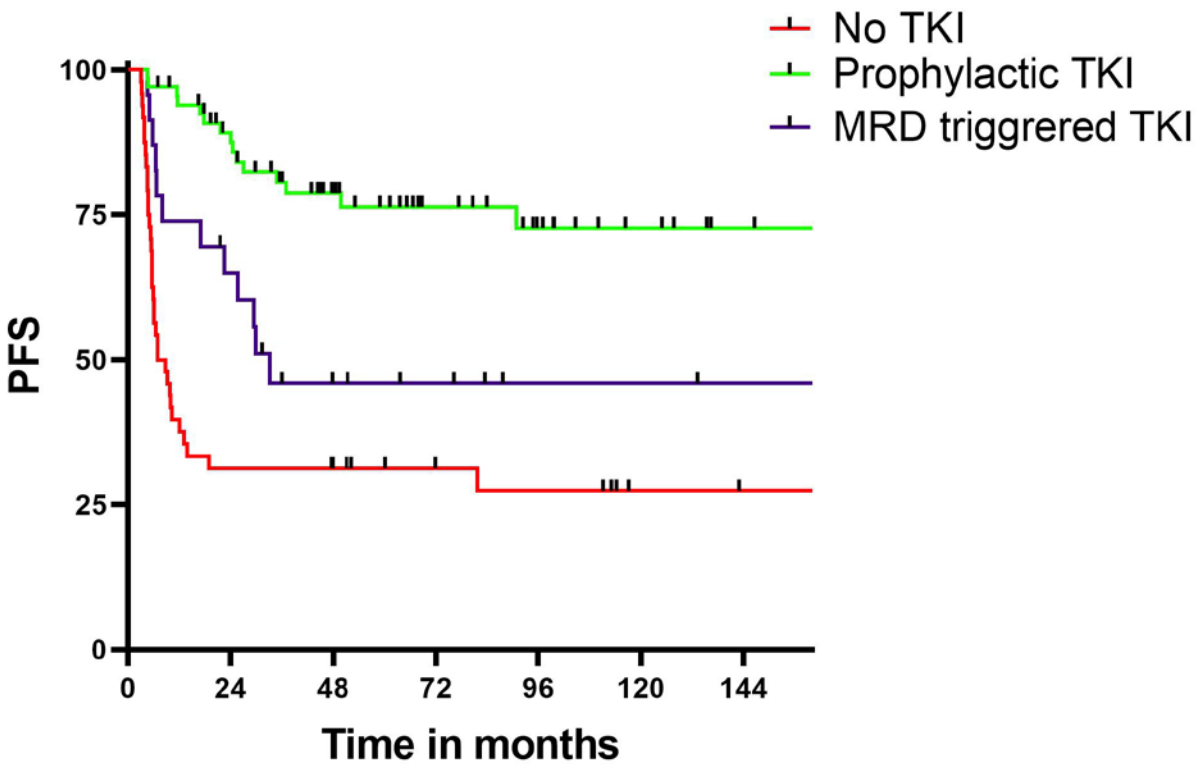
Impact of TKI maintenance on patients who were in CR and alive at three months post-transplant

In our cohort, 135 patients were in CR and remained alive without progression at approximately 3 months. 67 patients were started on prophylactic TKI within three months of transplant (group A). 23 patients were started on TKI after MRD became positive (MRD-triggered, group B). Total of 48 patients did not receive any TKI (group C). The median survival in group A, B and C were not reached, 33.1 months and 7.81 months, respectively (p-value = <0.0001).



In an allogeneic-transplant population, the retrospective comparison between a maintenance therapy group with a no-maintenance group is fraught with glaring biases. Patients who have poor performance status post-allo-HSCT or who have developed complications related to transplant such as GVHD, recurrent infections or poor count recovery are less able to receive TKI maintenance. We reasoned that the effects of early treatment-related mortality have mostly resolved by the 3-months mark, and the majority of relapses would not have yet occurred. An earlier time-point would cause adulteration of effect of treatment-related mortality/GVHD in both arms, and a later time-point would hide TKI-prevented relapses. To

keep our population homogeneous between two comparative arms, we decided to elect 3 months as the most appropriate time-point when effects of non-relapse mortality and other issues as explained above will have lesser impact on patient's selection in one arm versus another. Therefore, above analysis can be misleading and to truly analyze the impact of TKI, we compared only those patients who were in CMR at the time of transplant and remained in CMR at three months post-transplant (please see the analysis in the main manuscript).

Table S1. Univariate and multivariate analysis of Cumulative Incidence of Relapse (CIR)

Covariates	Univariate Analysis		Multivariate analysis	
	HR (95% CI)	p-value	HR (95% CI)	p-value
Type of transplant -Cord/Haplo -Matched related / unrelated	1.23 (0.49 – 3.04)	0.65		
Disease status at transplant - CR ≥2 - CR 1	3.06 (1.5 – 6.26)	0.002	**3.36** **(1.54 – 7.32)**	**0.002**
Age (years) - 40 - >40	.646 (0.3 – 1.3)	0.23		
Molecular status at transplant - others - CMR	2.4 (1.06 – 5.42)	0.035	**2.5** **(1.09 – 5.71)**	**0.03**
Cytogenetics status - Ph+ alone - Ph+ plus other cyto. abnl.	.269 (0.11 – 0.63)	0.003	**0.3** **(0.133 – 0.70)**	**0.006**
Sex - Female - Male	0.85 (.41 – 1.77)	0.6		
HCT- CI - 0 - > 0	0.98 (0.37 – 2.6)	0.974		
Karnofsky - ≥90 - <90	1.29 (0.54 – 3.0)	0.55		
Conditioning regimen - Reduced Intensity - Myeloablative	1.26 (0.33 – 5.34)	0.746		

Table S2

Patient characteristics

This table includes patients who were in CMR at the time of transplant and remained alive in CMR at three months after transplant. Among this cohort, 18 received prophylactic TKI (group A). Patients in group B either did not receive TKI or received TKI after three months of transplant.

Patient characteristics	Prophylactic TKI n=18	No or delayed TKI n=24	p value
Median Age (Range) in years			0.175
Age upto 40	11	10	
Age >40	7	14	
Sex			0.627
Male	12	16	
Female	6	8	
Cytogenetics at diagnosis			0.428
Ph alone	13	14	
Ph plus other cytogenetics	5	8	
Unknown* n=2		2	
Karnofsky Score			0.082
>=90	16	18	
<90	2	4	
Disease status at allo-HCT,			0.059
CR1	17	17	
CR2	1	6	
CR3+	0	1	
Presence of MRD at HSCT, BCR-ABL (RT-PCR)			selection variable
CMR	18	24	
Transplant conditioning			0.571
Myeloablative	18	23	
Reduced-intensity	0	1	
Donor type			0.44
MRD	10	9	
MUD	5	10	
MMUD	0	2	
Haploidentical	1	2	
Cord	2	1	

Table S3.

Median duration of maintenance for each TKI

TKIs	Number	Median in days	Range in days
Imatinib	38	373	10 -2222
Dasatinib	31	497	7 - 1945
Ponatinib	11	460	97-1504
Bosutinib	1	1062	n/a
Nilotinib	1	124	n/a

Table S4

Table below presents individual data on 21 patients whose TKI was stopped because of disease relapse.

Patient Number	TKI Drug	Disease response prior to transplant	Time to TKI initiation after transplant (in days)	Duration of TKI before relapse (in days)
1	Imatinib	CR1	26.00	461.00
2	Imatinib	CR1	155.00	11.00
3	Imatinib	CR1	72.00	106.00
4	Imatinib	CR1	61.00	78.00
5	Imatinib	CR2	370.00	338.00
6	Imatinib	PD	90.00	34.00
7	Imatinib	CR1	40.00	37.00
8	Imatinib	CR1	35.00	620.00
9**	Imatinib switched to Dasatinib	CR1	48.00	132.00
10	Imatinib	CR2	57.00	14.00
11	Imatinib	CR 2	79.00	10.00
12**	Imatinib switched to Dasatinib	CR1	42.00	562.00
13**	Imatinib switched to Dastinib	CR1	84.00	216.00
14	Dasatinib	CR2	184.00	215.00
15	Dasatinib	CR1	47.00	302.00
16**	Dasatinib switched to ponatinib	CR2	81.00	16.00
17	Dasatinib	CR2	44.00	11.00
18**	Imatinib switched to Ponatinib to Bosutinib	CR1	161.00	652.00
19	Dasatinib	CR1	62.00	168.00
20	Dasatinib	CR2	126.00	7.00
21**	Dasatinib switched to bosutinib	CR1	38.00	339.00

*** CR1: complete response 1, CR2: complete response 2, PD -progressive disease

TKI stopped in 21 patients due to disease relapse. Number of relapses in individual TKI is below: Imatinib = 10; Dasatinib = 5; Combination of TKI = 6

**Patients were switched from one to another TKI due to intolerance.

The median time to relapse in those patients who stopped TKI for reasons other than relapse (excluding patients who suffered non-relapse mortality) was 146 days (range 36 – 746).