Supplemental materials

Supplemental Figure 1. Survival analysis according to renal involvement. Kaplan-Meier estimations of overall survival for patients with and without renal dysfunction at the diagnosis of TA-TMA. Concomitant renal dysfunction was significantly associated with an adverse overall survival (log-rank $P < 0.0001$).

Supplemental Figure 2. Survival analysis according to the independent prognostic factors in the derivation cohort. Kaplan-Meier estimations showed significantly different overall survival for patients with and without these prognostic factors (log rank $P < 0.001$ for each).

Supplemental Figure 3. ROC curve for the BATAP model. ROC curves showed good discriminative performance in both the derivation (AUC = 0.807, 95% CI 0.756-0.859) (A) and the validation (AUC = 0.766, 95% CI 0.707-0.826) (B) cohorts.

Supplemental Figure 4. Sensitivity analysis of the BATAP risk score revealing similar discriminative capacity in patients undergoing different transplant protocols. Patients undergoing other protocols included 51 patients receiving HLA-matched related donor transplantation and 7 patients receiving HLA-matched unrelated donor transplantation. AuROC (95%CI): 0.785 (0.745-0.824) for the total cohort, 0.794 (0.753-0.835) for the ATG-based group, and 0.749 (0.646-0.853) for the group of other protocols.

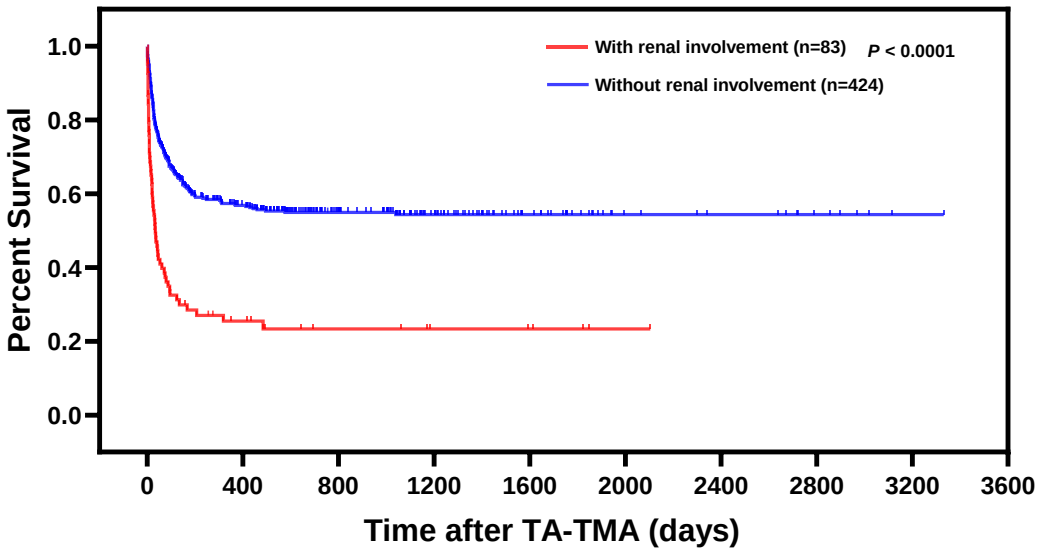
Supplemental Figure 5. Multivariate analysis exploring the prognostic effect of immunosuppressive modulations in the derivation cohort. Multivariate logistic regression showed no significant differences in the 6-month overall survival rates among patients undergoing different immunosuppressive regimens after the TMA diagnosis. Subgroup analysis focusing on the BATAP intermediate/high-risk groups and the BATAP low-risk group also showed no significant differences. *For each group, the reference group consisted of patients undergoing maintenance of CNIs or switch to other CNIs (n=124 (46.1%) in the total group; n=47 (41.4%) in the BATAP intermediate/high-risk group; and n=47 (56.6%) in the BATAP low-risk group). **Adjusted by sex, age, aGVHD and BATAP risk group. #Adjusted by sex, age and aGVHD.

Supplemental Figure 6. Fine-Gray model for nonrelapse mortality (NRM) in patients with different immunosuppressant modulations. Patients undergoing withdrawal of CNIs showed adverse NRM (A, log-rank *P* = 0.016). However, when stratified by the BATAP risk groups (B, the BATAP intermediate/high-risk groups, log-rank *P* = 0.476; C, the BATAP low-risk group, log-rank *P* = 0.126), subgroup analysis showed no significant differences.

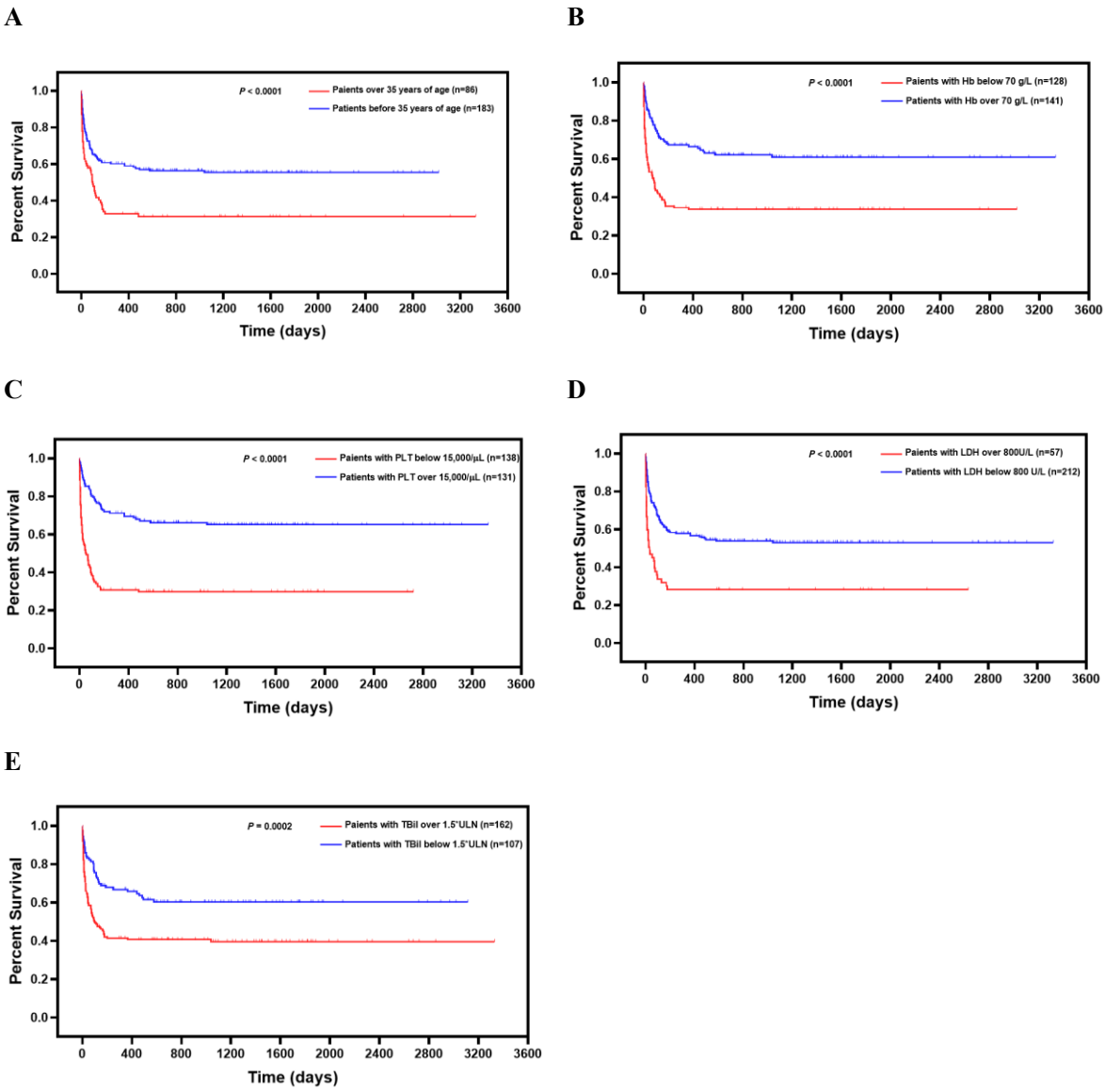
Supplemental Table 1. Univariate analysis identifying the potential prognostic factors

Supplemental Table 2. The predicted and observed probabilities for 6-month mortality of TA-TMA

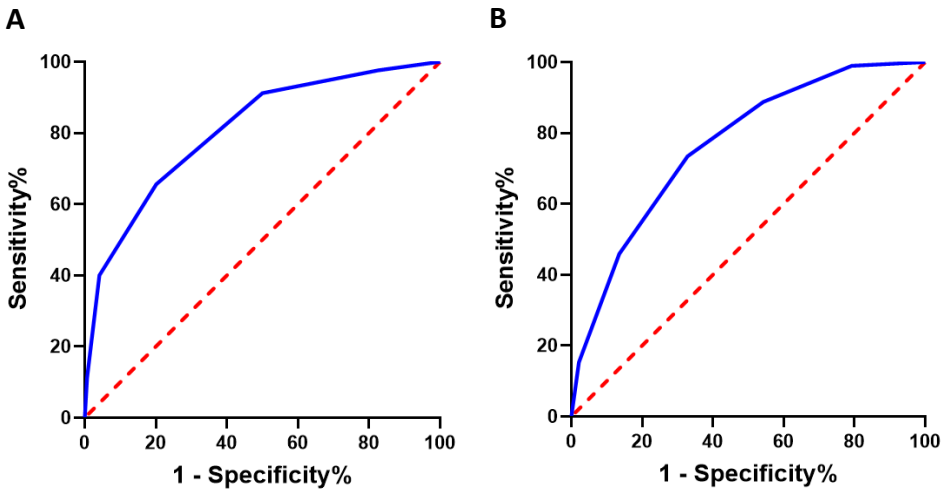
Supplemental Table 3. Characteristics and outcomes of the patients receiving different immunosuppressive regimens after TA-TMA



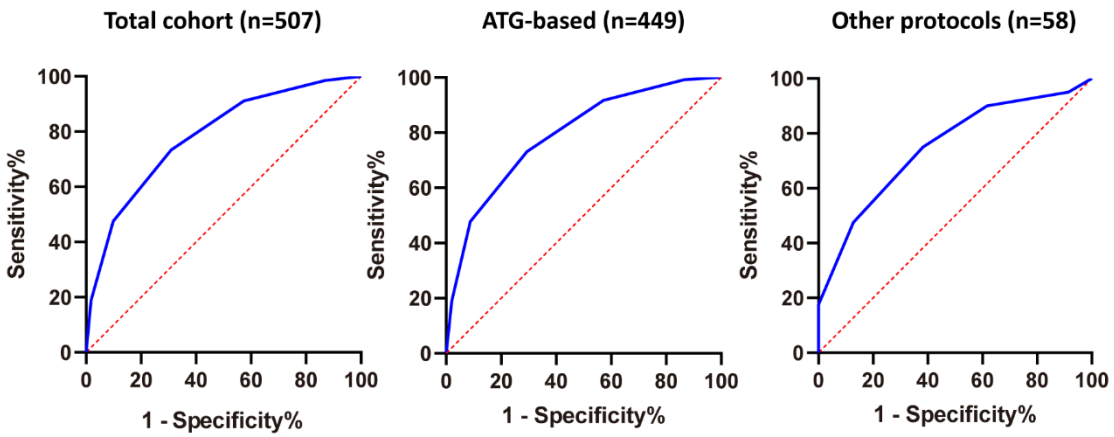
Supplemental Figure 1. Survival analysis according to renal involvement. Kaplan-Meier estimations of overall survival for patients with and without renal dysfunction at the diagnosis of TA-TMA. Concomitant renal dysfunction was significantly associated with an adverse overall survival (log-rank $P < 0.0001$).



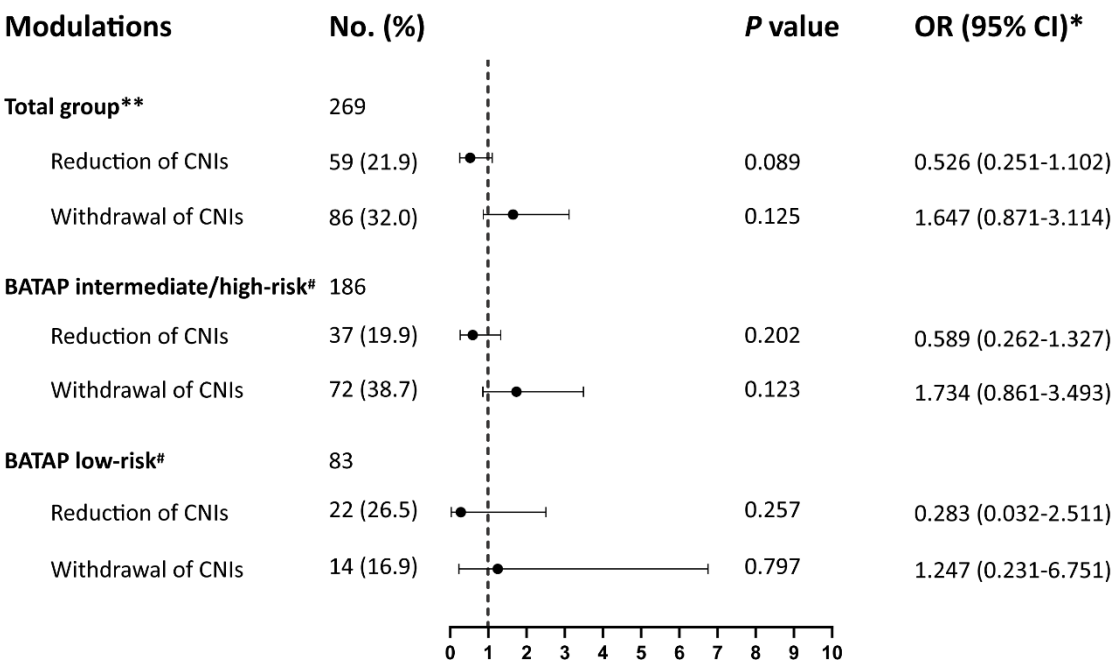
Supplemental Figure 2. Survival analysis according to the independent prognostic factors in the derivation cohort. Kaplan-Meier estimations showed significantly different overall survival for patients with and without these prognostic factors (log rank $P < 0.001$ for each).



Supplemental Figure 3. ROC curve for the BATAP model. ROC curves showed good discriminative performance in both the derivation (AUC = 0.807, 95% CI 0.756-0.859) (A) and the validation (AUC = 0.766, 95% CI 0.707-0.826) (B) cohorts.



Supplemental Figure 4. Sensitivity analysis of the BATAP risk score revealing similar discriminative capacity in patients undergoing different transplant protocols. Patients undergoing other protocols included 51 patients receiving HLA-matched related donor transplantation and 7 patients receiving HLA-matched unrelated donor transplantation. AuROC (95%CI): 0.785 (0.745-0.824) for the total cohort, 0.794 (0.753-0.835) for the ATG-based group, and 0.749 (0.646-0.853) for the group of other protocols.

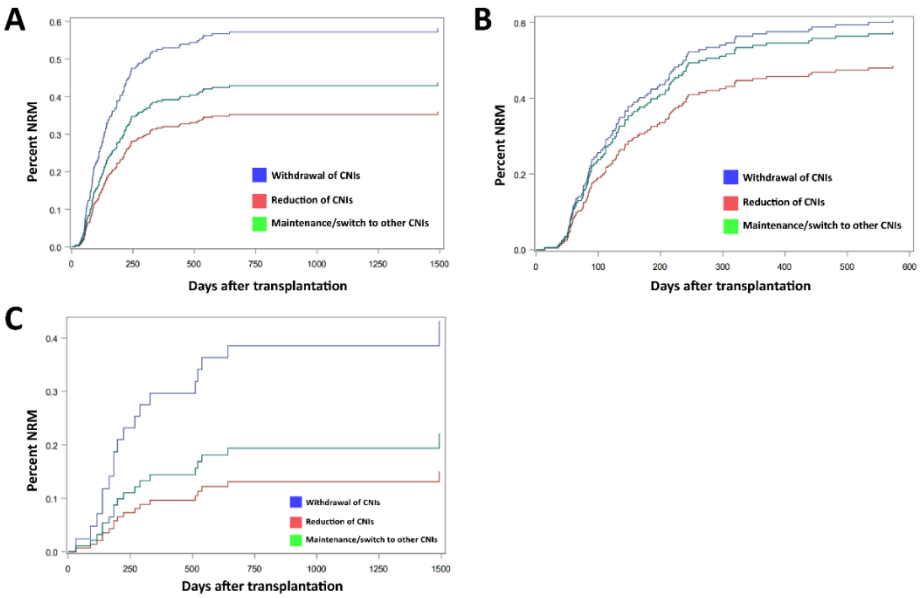


Supplemental Figure 5. Multivariate analysis exploring the prognostic effect of immunosuppressive modulations in the derivation cohort. Multivariate logistic regression showed no significant differences in the 6-month overall survival rates among patients undergoing different immunosuppressive regimens after the TMA diagnosis. Subgroup analysis focusing on the BATAP intermediate/high-risk groups and the BATAP low-risk group also showed no significant differences.

*For each group, the reference group consisted of patients undergoing maintenance of CNIs or switch to other CNIs (n=124 (46.1%) in the total group; n=47 (41.4%) in the BATAP intermediate/high-risk group; and n=47 (56.6%) in the BATAP low-risk group).

**Adjusted by sex, age, aGVHD and BATAP risk group.

#Adjusted by sex, age and aGVHD.



Supplemental Figure 6. Fine-Gray model for nonrelapse mortality (NRM) in patients with different immunosuppressant modulations. Patients undergoing withdrawal of CNIs showed adverse NRM (A, log-rank *P* = 0.016). However, when stratified by the BATAP risk groups (B, the BATAP intermediate/high-risk groups, log-rank *P* = 0.476; C, the BATAP low-risk group, log-rank *P* = 0.126), subgroup analysis showed no significant differences.

Supplemental Table 1. Univariate analysis identifying the potential prognostic factors

Characteristics	**OR (95% CI)**	***P* value***
Sex (Male *vs.* Female)		0.342
Age at diagnosis (≥ 35 *vs.* < 35 years)	2.476 (1.463-4.190)	0.001
HCT-CI		
1-2 *vs.* 0		0.390
≥ 3 *vs.* 0		0.388
Underlying disease		
AML (with *vs.* without)	1.673 (1.011-2.769)	0.045
ALL (with *vs.* without)		0.972
CML (with *vs.* without)		0.506
MDS/MPN (with *vs.* without)		0.148
Others (with *vs.* without)		0.214
Donor type		
Partially matched related *vs.* Matched related		0.424
Matched unrelated *vs.* Matched related		0.767
ABO mismatched *vs.* ABO matched		0.907
Conditioning regimen		
BU/CY (yes *vs.* no)		0.281
BU/CY+ATG (yes *vs.* no)		0.995
TBI-based regimen (yes *vs.* no)		0.403
Other (yes *vs.* no)		0.403
GVHD prophylaxis		
Tacrolimus/sirolimus (yes *vs.* no)		0.130
Donor lymphocyte infusion (with *vs.* without)		0.866
Hb < 70 g/L	4.063 (2.443-6.758)	<0.0001
Platelet count < 15,000/μL	6.004 (3.540-10.182)	<0.0001
TBIL > 1.5*ULN	2.947 (1.761-4.931)	<0.0001
Hypoalbuminemia (with *vs.* without)	2.122 (1.239-3.637)	0.006
Proteinuria (with *vs.* without)	3.133 (1.876-5.231)	<0.0001

Supplemental Table 2. The predicted and observed probabilities for 6-month mortality of TA-TMA

Risk score	Estimated risk	Observed frequency	
		Derivation cohort (n=269)	Validation cohort (n=238)
0	0.073509	0.107143 (3/28)	0.033333 (1/30)
1	0.153683	0.145455 (8/55)	0.222222 (10/45)
2	0.293592	0.426667 (32/75)	0.333333 (15/45)
3	0.487503	0.581818 (32/55)	0.5 (27/54)
4	0.685249	0.878049 (36/41)	0.652174 (30/46)
5	0.832855	0.9333333 (14/15)	0.8333333 (15/18)

Supplemental Table 3. Characteristics and outcomes of the patients receiving different immunosuppressive regimens after TA-TMA

Characteristics	Management of CNIs			*P* value
	Withdrawal (n=86)	Reduction (n=59)	Switch / Maintenance (n=124)	
Sex, n (%)				NS
Male	49 (57.0)	36 (61.0)	76 (61.3)	
Female	37 (43.0)	23 (39.0)	48 (38.7)	
Age at HSCT (years)				NS
Median [range]	23.5 [8-62]	25 [3-56]	28.5 [4-59]	
Donor type, n (%)				NS
Matched related	11 (12.8)	6 (10.2)	11 (8.9)	
HLA-partially matched related	74 (86.0)	53 (89.8)	112 (90.3)	
Matched unrelated	1 (1.2)	0	1 (0.8)	
HCT-CI, n (%)				NS
0	63 (73.3)	45 (76.3)	88 (71.0)	
1-2	21 (24.4)	14 (23.7)	31 (25.0)	
≥ 3	2 (2.3)	0	5 (4.0)	
Age at TA-TMA diagnosis (years)				NS
Median [range]	24 [8-62]	25 [3-56]	28.5 [4-59]	
Immunosuppression prior to TMA				NS
CsA-based	59 (68.6)	44 (74.6)	98 (79.0)	
Tacrolimus/sirolimus	27 (31.4)	15 (25.4)	26 (21.0)	
BATAP risk group, n (%)				0.001
Low-risk (<2 pts)	14 (16.3)	22 (37.3)	47 (37.9)	
Intermediate/high-risk (≥2 pts)	72 (83.7)	37 (62.7)	77 (62.1)	
aGVHD, n (%)				
None	20 (23.2)	18 (30.5)	34 (27.4)	0.343
I-II	40 (46.5)	30 (50.8)	65 (52.4)	0.697
III-IV	26 (30.2)	11 (18.6)	25 (20.2)	0.155
Infection at TMA onset, n (%)				
Bacteremia	6 (7.0)	4 (6.8)	10 (8.1)	0.935
Viremia	21 (24.4)	15 (25.4)	28 (22.6)	0.902

Fungal	4 (4.7)	3 (5.1)	7 (5.6)	0.949
Infection within 6-mo of TMA, n (%)				
Bacteremia	9 (10.5)	5 (8.5)	13 (10.5)	0.903
Viremia	14 (16.3)	11 (18.6)	26 (21.0)	0.694
Fungal	9 (10.7)	7 (11.9)	14 (11.3)	0.964
Relapse, n (%)	8 (9.3)	2 (3.4)	11 (8.9)	0.357
6-mo overall survival	37.2% (32/86)	69.5% (41/59)	57.3% (71/124)	<0.001
Overall survival	33.7% (29/86)	64.4% (38/59)	51.6% (64/124)	0.001
Nonrelapse mortality	58.1% (50/86)	35.6% (21/59)	41.1% (51/124)	0.012

Abbreviations: TA-TMA, transplant-associated thrombotic microangiopathy; HSCT, hematopoietic stem cell transplantation; HLA, human leukocyte antigen; BU, busulfan; CY, cyclophosphamide; TBI, total body irradiation; GVHD, graft-versus-host disease; CsA, cyclosporine