SUPPLEMENTARY MATERIAL

Association between elevated white blood cell counts and thrombotic events in polycythemia vera: Analysis from REVEAL

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SUPPLEMENTAL TABLE 1 Anticoagulant medications at enrollment by history of TEs.

	With History of TE (n=456)	**Without History of TE (n=1815)**	**All (N=2271)**
Patients who took at least one medication at enrollment, n (%)	168 (36.8)	94 (5.2)	262 (11.5)
Apixaban	10 (2.2)	12 (0.7)	22 (1.0)
Rivaroxaban	34 (7.5)	17 (0.9)	51 (2.2)
Dabigatran	2 (0.4)	14 (0.8)	16 (0.7)
Enoxaparin	14 (3.1)	4 (0.2)	18 (0.8)
Fondaparinux	4 (0.9)	0	4 (0.2)
Vitamin K Antagonists	109 (23.9)	48 (2.6)	157 (6.9)

TE, thrombotic event.

SUPPLEMENTAL TABLE 2 Hematocrit status, white blood cell count status, and platelet count at enrollment.

Variable	Low Risk PV n = 503	High Risk PV n = 1768	All patients (N = 2271)
Hematocrit status, n (%)			
≤45%	213 (42.3)	902 (51.0)	1115 (49.1)
>45%	260 (51.7)	748 (42.3)	1008 (44.4)
NR	30 (6.0)	118 (6.7)	148 (6.5)
WBC×10^9/L status, n (%)			
≤11	328 (65.2)	1129 (63.9)	1457 (64.2)
>11	137 (27.2)	511 (28.9)	648 (28.8)
NR	38 (7.6)	128 (7.2)	166 (7.3)
Platelet count ×10^9/L, n (%)			
≤400	285 (56.7)	1050 (59.4)	1335 (58.8)
>400	179 (35.6)	583 (33.0)	762 (33.6)
NR	39 (7.8)	135 (7.6)	174 (7.7)

NR, not recorded.

SUPPLEMENTAL TABLE 3 Number of TEs during the study by PV risk.

Number of TEs, n (%)	Low Risk PV n = 503	High Risk PV n = 1768	All patients (N = 2271)
0	489 (97.2)	1676 (94.8)	2165 (95.3)
1	13 (2.6)	73 (4.1)	86 (3.8)
2	1 (0.2)	12 (0.7)	13 (0.6)
3	0	5 (0.3)	5 (0.2)
4	0	1 (0.1)	1 (<0.1)
5	0	1 (0.1)	1 (<0.1)

PV, polycythemia vera; TE, thrombotic event.

SUPPLEMENTAL TABLE 4 Summary of all TEs during the study.

	All patients (N = 2271)
Total TEs, n (%)	**142 (6.3)**
Arterial TEs, n (%)	**42 (1.8)**
Transient ischemic attack	15 (0.7)
Acute myocardial infarction	7 (0.3)
Arterial thrombosis	5 (0.2)
Cerebrovascular accident	3 (0.1)
Peripheral artery thrombosis	3 (0.1)
Aortic thrombosis	1 (<0.1)
Acute coronary syndrome	1 (<0.1)
Amaurosis fugax	1 (<0.1)
Arterial thrombosis	1 (<0.1)
Atrial thrombosis	1 (<0.1)
Coronary artery thrombosis	1 (<0.1)
Colitis ischemic	1 (<0.1)
Peripheral embolism	1 (<0.1)
Other*	2 (0.1)
Venous TEs, n (%)	**100 (4.4)**
Deep vein thrombosis	43 (1.9)
Pulmonary embolism	25 (1.1)
Thrombophlebitis superficial	11 (0.5)
Intracranial venous sinus thrombosis	5 (0.2)
Portal vein thrombosis	4 (0.2)
Splenic vein thrombosis	4 (0.2)
Retinal vein thrombosis	2 (0.1)
May-Thurner syndrome	1 (<0.1)
Intracardiac thrombus	1 (<0.1)
Thrombosis in device	1 (<0.1)
Venoocclusive disease	1 (<0.1)
Other†	2 (0.1)

*2 other events were reported as arterial TEs and qualified by investigator as abdominal wall hematoma and international normalized ratio increased.

†2 other events were reported as venous TEs and qualified by investigator as hematoma and pleural effusion.

TE, thrombotic event.

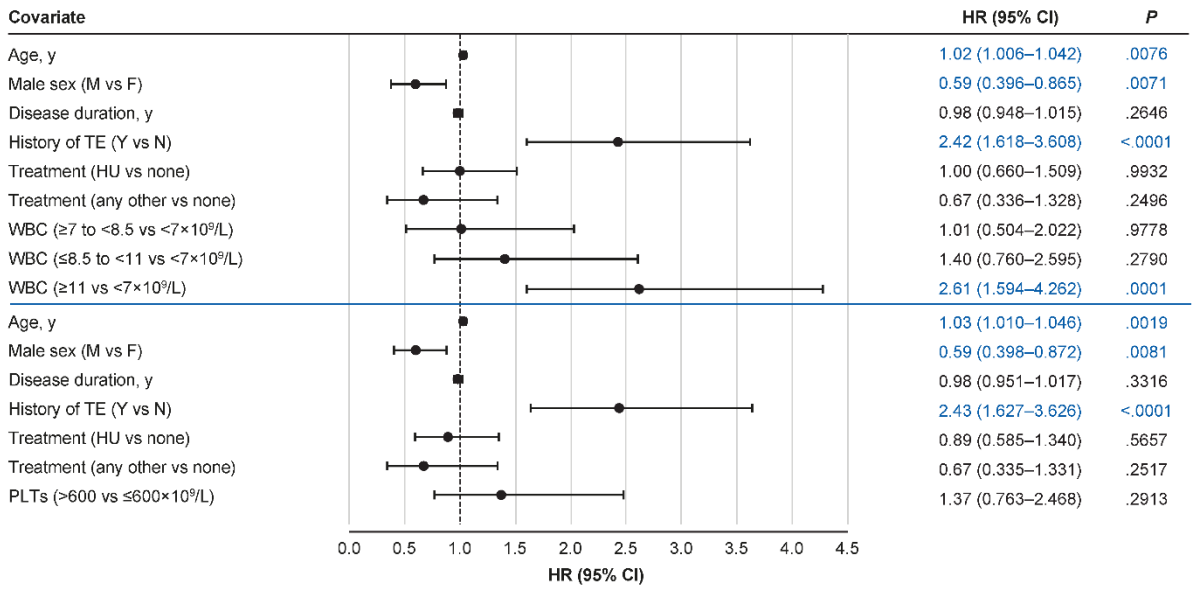
SUPPLEMENTAL TABLE 5 Studies of the association between WBC count and TE risk.

First author	N	Analysis description	Comparison ($\times 10^9$/L)	Result*	*P* value
Ronner L. et al.[†]	520	• Retrospective, group-based trajectory modeling • Multivariate, time-dependent covariate Cox proportion hazards model	10 vs 5 15 vs 5 35 vs 5	2.32 (0.86-6.27) 1.83 (0.54-6.21) 2.43 (0.26-22.35)	.0957 .3340 .4333
Landolfi R. et al.[‡]	1638	• Multivariate, time-dependent covariate Cox proportion hazards model	10.1 to 15.0 vs ≤10 >15 vs ≤10	1.00 (0.67-1.48) 1.56 (1.05-2.30)	.986 .028
Parasuraman S. et al.[§]	1565	• Multivariate, time-proportionate Cox proportion hazards model	<7.0 vs 7.0 to 8.4 <7.0 vs 8.5 to <11 <7.0 vs ≥11	1.10 (0.82-1.48) 1.47 (1.10-1.96) 1.87 (1.44-2.43)	.5395 .0097 <.0001
Alvarez- Larrán A. et al.[¶]	261	• Incidence rates of TEs from retrospective chart review data	<10 vs ≥10	30.3 vs 41.4	.4000

*Results for each study are presented as HR (95% CI), except for Alvarez-Larran A. et al, where results are presented as incidence rate of TEs x 1000 person-years. [†]Ronner L, et al. *Blood*. 2020;135(19):1696-1703; [‡]Landolfi R, et al. *Blood*. 2007;109(6):2446-2452; [§]Parasuraman S, et al. *Clin Lymphoma Myeloma Leuk*. 2020;20(2):63-69; [¶]Alvarez-Larrán A, et al. *Blood*. 2012;119(6):1363-1369.

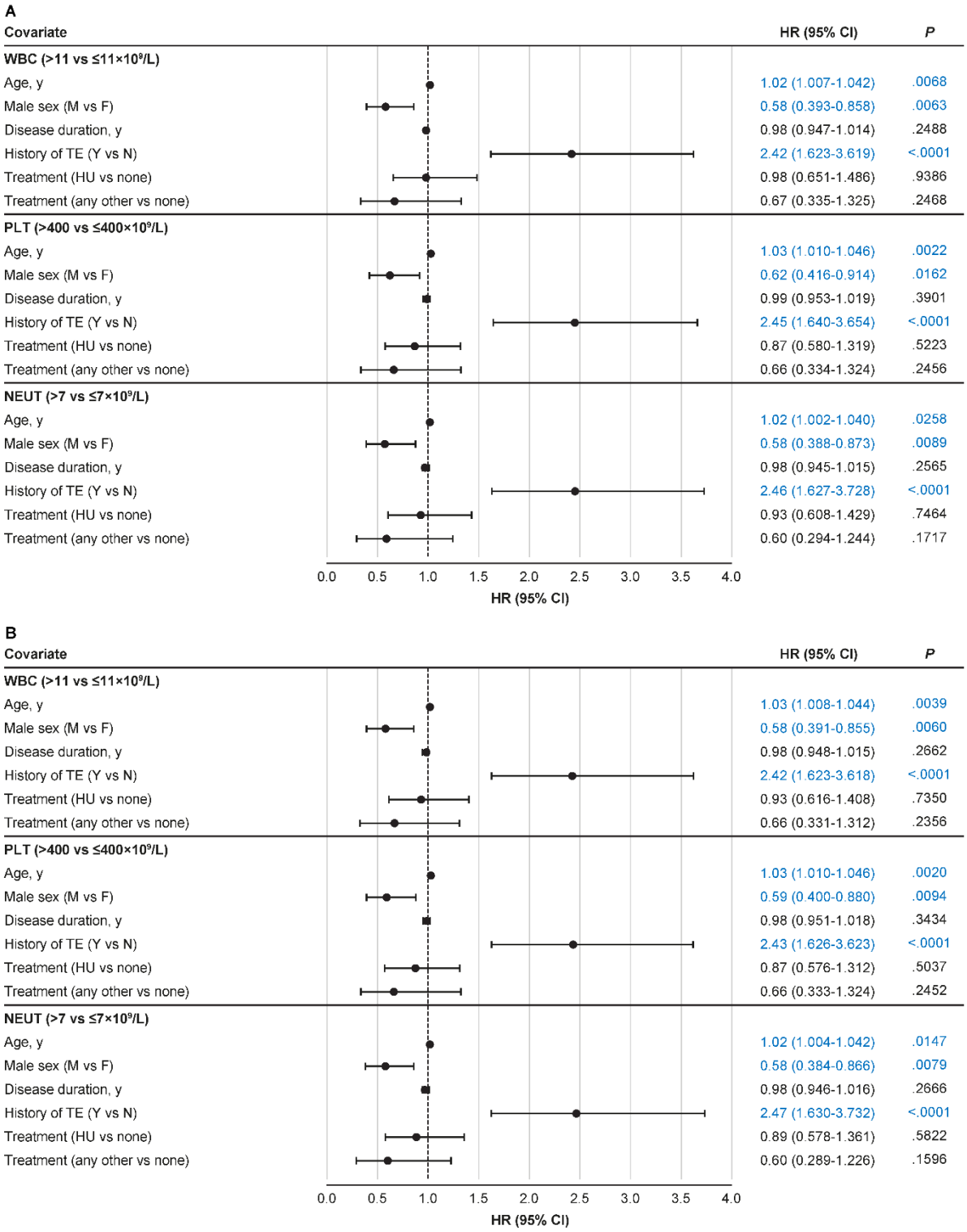
CI, confidence interval; HR, hazard ratio; HCT, hematocrit.

SUPPLEMENTAL FIGURE 1 Association between blood counts and TEs using alternative thresholds of WBC count (WBC $<7\times10^9$/L; $7\times10^9 \leq$ WBC $<8.5\times10^9$/L; $8.5\times10^9 \leq$ WBC $<11\times10^9$/L; WBC $\geq11\times10^9$/L) and platelet count ($>600\times10^9$/L).



Significant values ($P < .05$) are indicated in blue font. Other treatments include ruxolitinib, anagrelide, interferon, busulfan, and chlorambucil. HU, hydroxyurea; PLT, platelet; TE, thrombotic event; WBC, white blood cell.

SUPPLEMENTAL FIGURE 2 Covariates of age, sex, disease duration, history of TE, and treatment for (A) isolated and (B) sustained elevation of WBC count (>11 x 10^9/L), platelet count (>400 x 10^9/L), and absolute neutrophil count (>7 x 10^9/L).



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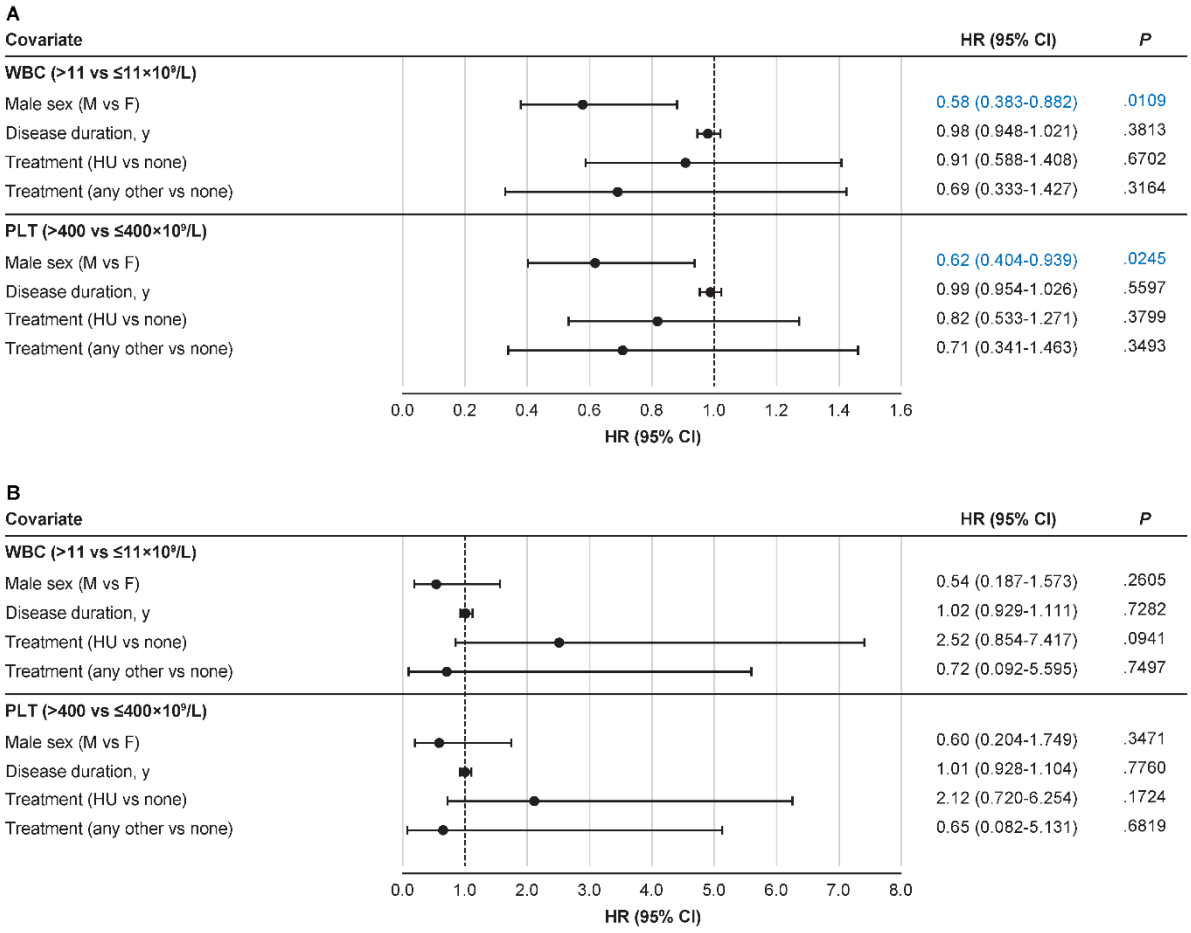
SUPPLEMENTAL FIGURE 3 Covariates of sex, disease duration, and treatment for acute elevation of WBC count (>11 x 10^9/L) and platelet count (>400 x 10^9/L), in patients with (A) high- and (B) low-risk PV.



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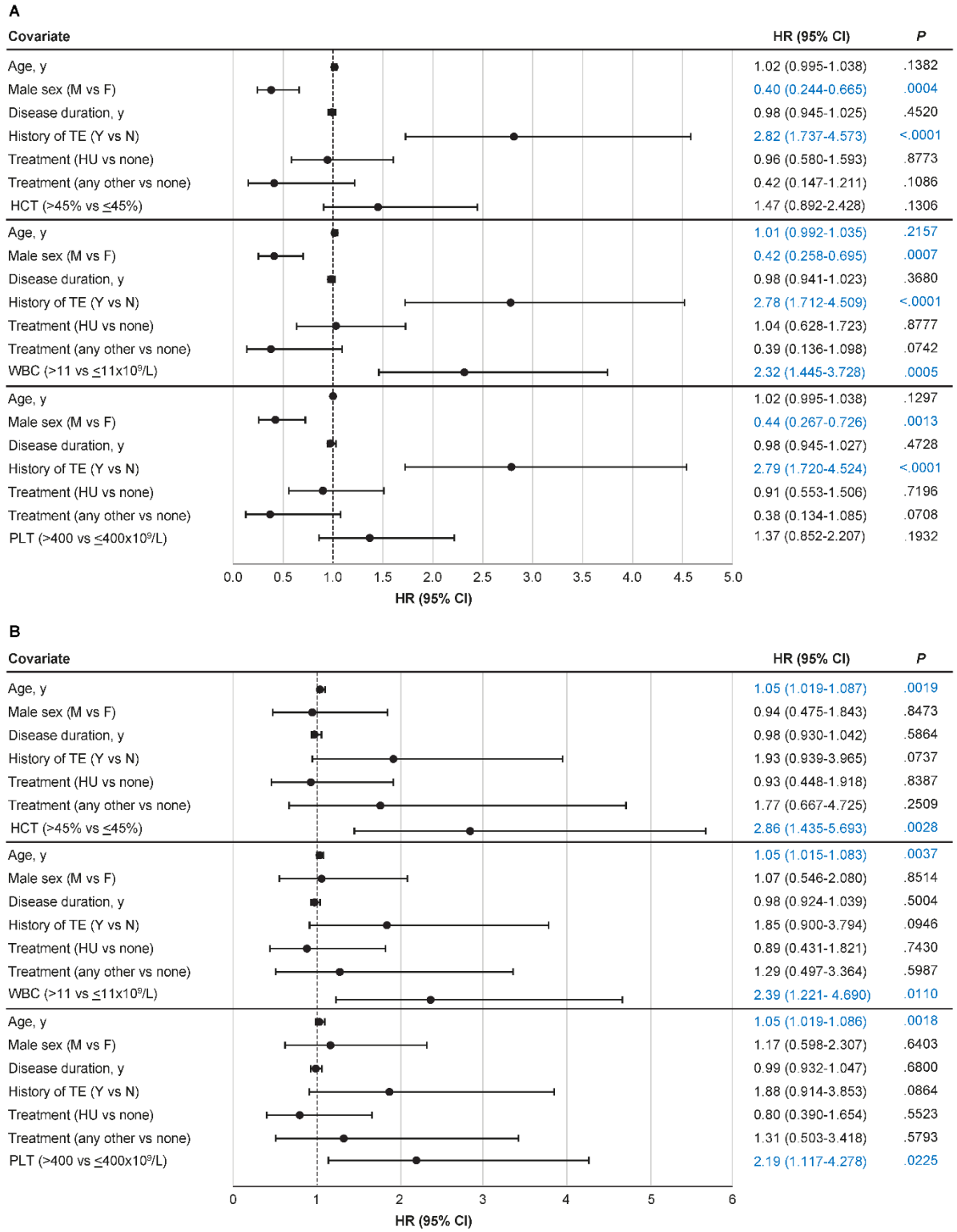
SUPPLEMENTAL FIGURE 4 Analysis of TE associations stratified by (A) venous and (B) arterial TEs.



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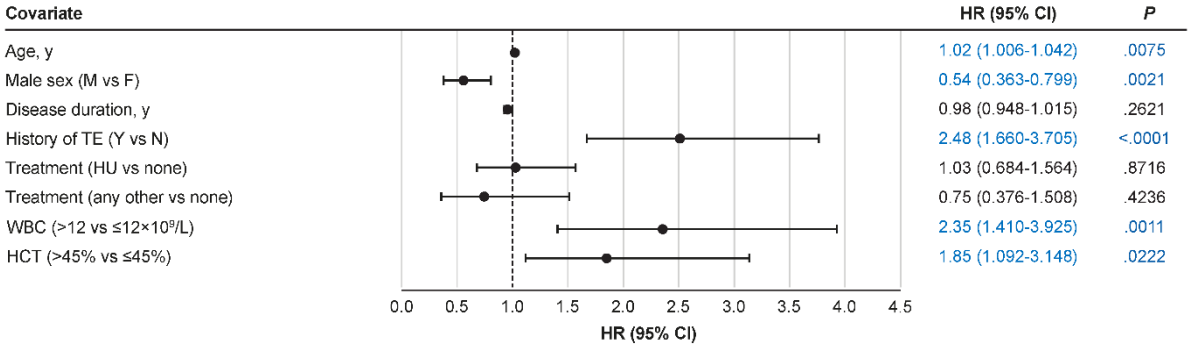
SUPPLEMENTAL FIGURE 5 Covariates of age, sex, disease duration, history of TE, and treatment for isolated WBC count elevation (>12×10^9/L). Significant values (P < .05) are indicated in blue font. HCT, hematocrit; TE, thrombotic event; WBC, white blood cell.



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