Supplemental Online Content

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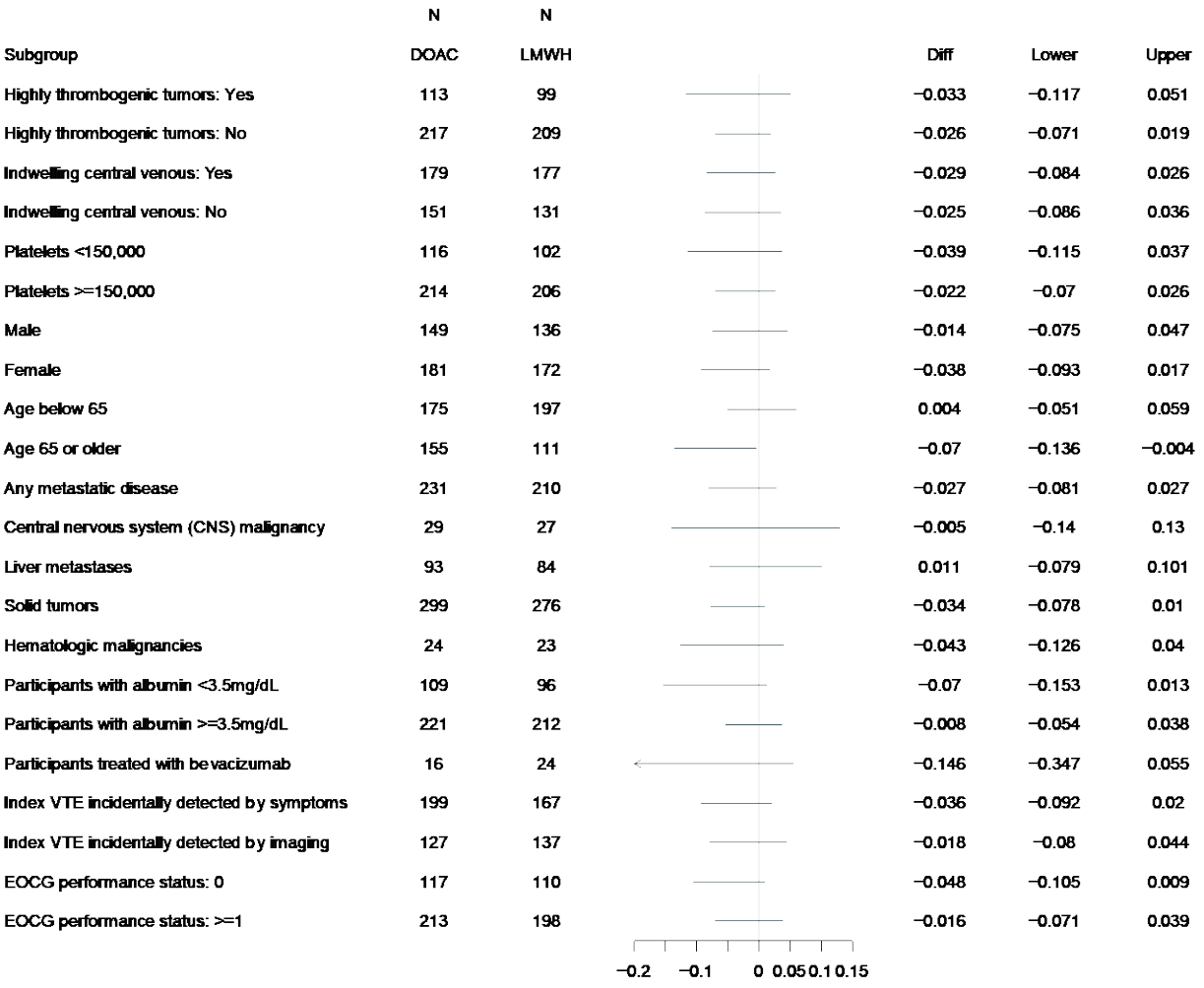
This supplemental material has been provided by the authors to give readers additional information about their work.

eTable 1. Adjusted Event Rates of Recurrent VTE, Death, and Major Bleeding at 6 Months in the Randomized Cohort by Generalized Linear Mixed-Effects Models

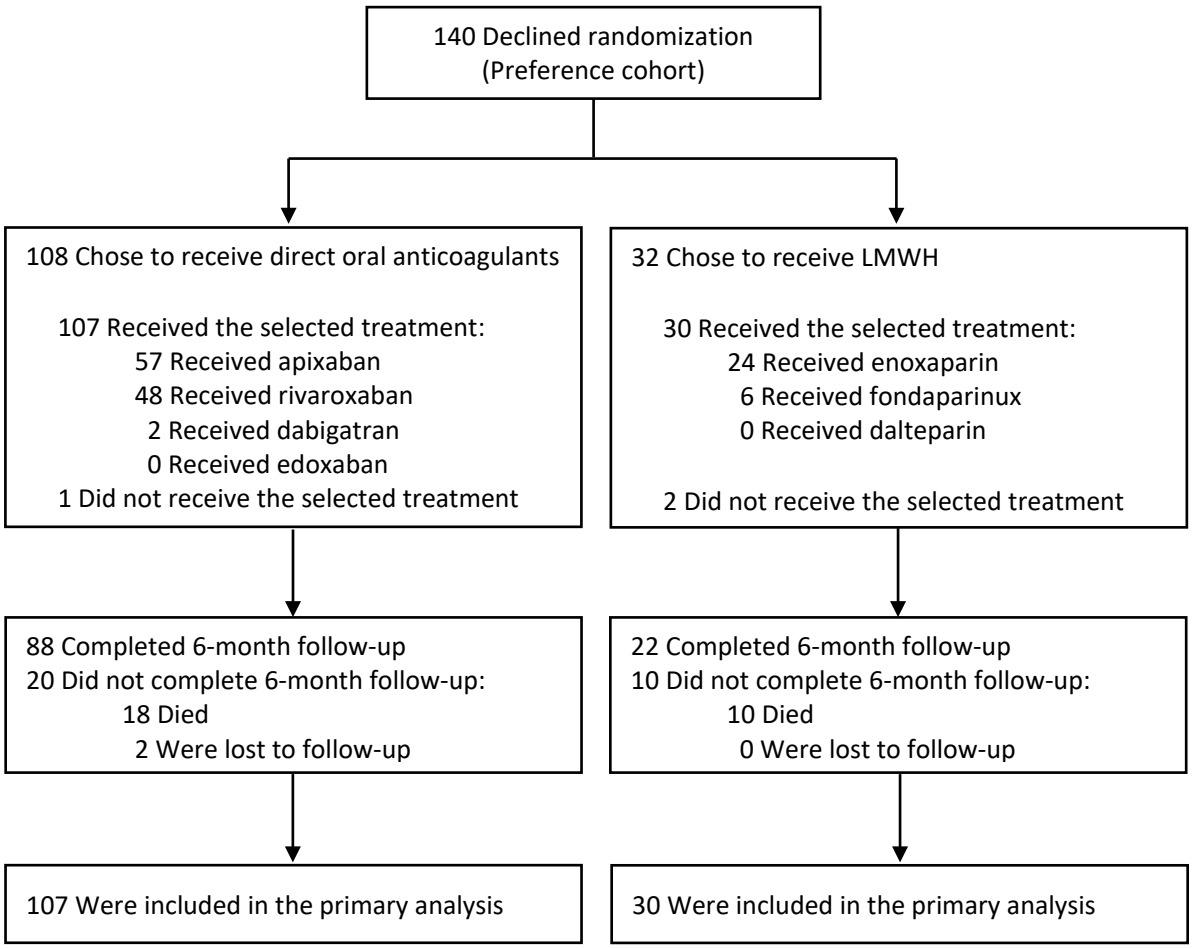
Endpoint	DOAC	LMWH	Difference	(0.95 confidence interval)	
			Estimate	one-sided	two-sided
Recurrent VTE (primary) [%]	6.0	8.7	-2.7	(-100, 0.8)	(-6.9, 1.5)
Death (event rate) [%]	20.8	18.0	2.8	NA	(-3.5, 9.2)
Major bleeding [%]	4.9	5.3	-0.4	(-100, 2.5)	(-3.8, 3.1)

eFigure 1. Forest Plot of the Likelihood of Recurrent VTE in Pre-defined Participant Subgroups in the Randomized Cohort



Abbreviations: DOAC, direct oral anticoagulants; LMWH, low molecular weight heparin; VTE, venous thromboembolism; ECOG; eastern cooperative oncology group. The horizontal lines show two-sided 0.95 confidence interval for the difference (DOAC versus LWMW) in cumulative incidence rate of recurrent VTE event at 6 months.

eFigure 2. Patient Dispositions in the Preference Cohort



eTable 2. Baseline Participant Characteristics in a Study of the Effect of Direct Oral Anticoagulants Versus Low Molecular Weight Heparins for Treatment of Venous Thromboembolic Events in Patients With Cancer (the Preference Cohort)

Characteristic	Direct Oral Anticoagulant (N = 107)	Low Molecular Weight Heparin (N = 30)
Age, median (q1, q3) , y	66 (58, 72)	67 (61, 72)
Age 65y or older (%)	62(58)	19(63)
Gender (%)		
Female	51(48)	18(60)
Male	56(52)	12(40)
Ethnicity (%)		
Not Hispanic or Latino	101(97)	28(100)
Hispanic or Latino	3(3)	0
Race (%)[a]		
White	90(86)	23(77)
Black or African American	12(11)	3(10)
Asian	2(2)	2(7)
American Indian or Alaskan Native	1(1)	1(3)
Native Hawaiian or Other Pacific Islander	0	1(3)
Education Level (%)		
Grade school or less	2(2)	2(7)
High school graduate or GED	18(17)	2(7)
Some vocational, business or trade school	7(7)	3(10)
Some college	27(26)	9(31)
College graduate and some graduate school but no degree	25(24)	8(28)
Graduate or professional degree	26(25)	5(17)
Body Mass Index, median (q1, q3)	27.4 (23.6, 30.9)	27.6 (24.7, 30.7)
Body Mass Index (%)		
Less than 18.5	3(3)	1(3)
18.5 to 24.9	33(31)	8(27)
25 to 29.9	38(36)	11(37)
30 or more	33(31)	10(33)
Smoking Status (%)		
Never Smoker	54(52)	13(46)
Former Smoker	43(41)	13(46)
Current Smoker	7(7)	2(7)

Participant reported functional status [ECOG Performance Status] (%)[b]		
0	53(50)	14(50)
1	39(36)	10(36)
>=2	15(14)	4(14)
Presence of Highly thrombogenic tumor (%)[c]	35(33)	11(37)
Presence of Indwelling central venous catheter (%)	64(60)	15(50)
Platelet Count [mm^3] (%)[d]		
Below 100,000	10(9)	4(13)
100,000-149,000	22(21)	2(7)
150,000-249,000	41(38)	13(43)
250,000-449,000	23(21)	7(23)
450,000 and above	11(10)	4(13)
Serum albumin [g/dL] (%)[e]		
Below 3.5	43(40)	12(40)
3.5 or above	64(60)	18(60)
Type of Cancer (%)		
Gastrointestinal	45(42)	11(37)
Breast	14(13)	4(13)
Lung	14(13)	2(7)
Lymphoma/Multiple Myeloma/CLL	14(13)	2(7)
Gynecologic	6(6)	9(30)
Genitourinary	6(6)	1(3)
Sarcoma	4(4)	0
Head and Neck	1(1)	0
Brain	1(1)	0
Skin/Melanoma	1(1)	0
Other cancer type[f]	1(1)	1(3)
Evidence of any metastatic/disseminated disease (%)[g]	64(60)	23(77)
Liver metastases	27	7
Lung metastases	23	5
Bone metastases	11	3
Brain metastases	2	2
Other metastases	27	14
Treatment with bevacizumab (%)	9(8)	6(20)
Type of index VTE (%)		
PE with or without DVT	57(53)	14(47)

DVT alone	49(46)	15(50)
Other type	1(1)	1(3)
Mode of presentation of index VTE (%)		
Presentation with symptoms or physical findings	69(64)	18(60)
Presentation detected on imaging	37(35)	12(40)
Uncertain	1(1)	0

Abbreviations: GED, general education development test; CLL, chronic lymphocytic leukemia; VTE, venous thromboembolism; PE, Pulmonary embolism; DVT, deep vein thrombosis.
Notes:

a. Race is based on patient's self-report recorded in the EHR.
b. ECOG performance status is a scale to assess the functional status of a patient. It was developed by the Eastern Cooperative Oncology Group and published in 1982. The score ranges from 0 to 5. The score 0 indicate the fully active and 5 indicates death.
c. Highly thrombogenic tumor: pancreas, lung, esophagus, and ovarian
d. Normal range of platelet count: 150,000-450,000 per mcL
e. Normal range of serum albumin: 3.5-5.4 gm/dL
f. Other cancer type: Chordoma (Direct Oral Anticoagulant group), Peritoneal cancer (Low Molecular Weight Heparin group)
g. Evidence of any metastatic disease: the metastatic locations are not mutually exclusive.

eTable 3. Clinical Outcomes at 6 Months in the Preference Cohort

Cohort	Endpoint	Direct oral anticoagulant	Low molecular weight heparin	Difference		
				Estimate	1-sided 0.95 CI	2-sided 0.95CI
Preference Cohort[a]	N	107	30			
	Non-fatal VTE[b]					
	Recurrent VTE [%]	7.5	4.1	3.3	(-100, 9.7)	(-4.3, 10.9)
	Mortality					
	Death [%]	16.3	23.8	-7.5	NA	(-20.9, 5.9)
	Restricted mean survival time[c] [day]	166	160	6	NA	(-11, 24)
	Bleeding					
	Major bleeding[d] [%]	11.5	7.6	3.9	(-100, 13.7)	(-7.8, 15.6)
	Clinically relevant non-major bleeding[e] [%]	5.0	1.1	3.9	NA	(-0.8, 8.6)
	Nuisance bleeding[f] [%]	14.0	11.5	2.5	NA	(-14.2, 19.2)
	Adverse events safety endpoint					
	Any serious adverse events[g] [%]	50.5	45.2	5.2	NA	(-6.9, 17.3)
	Severe serious adverse events[h] [%]	48.7	42.5	6.2	NA	(-6.4, 18.8)

Abbreviations: CI, confidence interval; VTE, venous thromboembolism.

a. Adjusted by propensity score weighting
b. Only VTEs that were non-fatal were considered because of the challenges of attributing cause of death in cancer patients to tumor progression versus VTE. Deaths irrespective of cause were considered as a secondary endpoint
c. The truncation time 180 days was used for calculation of the restricted mean survival time, which is interpreted as 180-day lifetime expectancy
d. Major bleeding was defined as Grade >=3 on the Common Terminology Criteria for Adverse Events from the National Cancer Institute (NCI CTCAE) criteria version 5. 0 (i.e., severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self care activities of daily living).
e. Clinically significant non-major bleeding was defined as Grade 2 on the NCI CTCAE criteria version 5.0
f. Nuisance bleeding was defined as Grade 1 on the NCI CTCAE criteria version 5.0
g. Any serious adverse events include VTE events and bleeding events of any grade
h. Severe serious adverse events are defined as Grade 3 or higher on the NCI CTCAE criteria version 5.0

eTable 4. Patient-Reported Outcomes in the Preference Cohort: Health-Related Quality of Life, Treatment Burden and Persistence With Anticoagulant Therapy

	Endpoint	Direct oral anticoagulant	Low molecular weight heparin	Difference (0.95 CI)
Preference Cohort[a]	N	107	30	
	N surveyed at 3 months[b]	77/99 (78%)	16/26 (62%)	
	N surveyed at 6 months[b]	75/89 (84%)	12/21 (57%)	
	Health-related QOL[c]			
	Change in physical health at 3 months[d]	3.4	1.8	1.6 (-7.5, 10.7)
	Change in physical health at 6 months[d]	2.7	-1.0	3.7 (-4.5, 11.8)
	Change in mental health at 3 months[d]	0.3	1.0	-0.7 (-6.1, 4.8)
	Change in mental health at 6 months[d]	0.6	0.4	0.2 (-5.9, 6.3)
	Anti-Clot Treatment Scale			
	Benefit[e] at 3 months	10.3	10.5	-0.3 (-1.8, 1.3)
	Benefit[e] at 6 months	11.3	10.3	1.0 (-0.5, 2.6)
	Burden[f] at 3 months	55.4	55.3	0.1 (-2.3, 2.4)
	Burden[f] at 6 months	54.2	52.5	1.8 (-1.7, 5.2)
	Persistence with anticoagulant therapy[g]			
	Assigned anticoagulant at 3 months [%]	86.7	79.5	7.2 (-8.6, 23.0)
	Assigned anticoagulant at 6 months [%]	74.3	60.2	14.1 (-5.3, 33.5)
	On any anticoagulant therapy at 3 months [%]	89.5	90.6	-1.1 (-13.0, 10.9)
	On any anticoagulant therapy at 6 months [%]	76.9	73.9	3.0 (-14.6, 20.6)

Abbreviations: CI, confidence interval; QOL, quality of life.

a. Adjusted by propensity score weighting

b. Respondents among non-deceased participants

c. Health-related quality of life was measured using the 12-Item Short Form Health Survey (SF-12) sub-scales for physical and mental health. Survey content included minor verbiage changes for clarity.

d. Change in score from baseline

e. The benefit scale has 3 items with scores from 3 to 15

f. The burden scale has12 items with scores from 12 to 60. Higher scores signify greater satisfaction (lower burden)

g. Participants who died prior to month 3 or 6 were considered persistent users if they were not known to have stopped treatment prior to death. Persistent use of anticoagulant therapy was ascertained based on both participant surveys and the electronic health record. ”Assigned anticoagulant” is defined as any of apixaban, dabigatran, edoxaban and rivaroxabn for the direct oral anticoagulant (DOAC) group and any of enoxaparin, dalteparin and fondaparinux for the low molecular weight heparin (LMWH) group. “Any anticoagulant therapy” is defined as any of those medication listed for DOAC and LMWH plus Warfarin. Patients who died or lost-to-follow-up at 3 (or 6) months were included in the denominator in calculating these proportions.

eTable 5. Propensity Score Model Used for Adjustment of Potential Confounding Factors in the Preference Cohort

	Odds Ratio	0.95CI	p-value
Intercept	5.96	(0.91, 38.99)	0.062
Age 65 or older vs. others	0.89	(0.33, 2.38)	0.820
Female vs. Male	0.45	(0.17, 1.16)	0.097
White vs. Non-White	2.03	(0.59, 6.94)	0.258
Collage grad or higher vs. others	1.27	(0.50, 3.22)	0.613
BMI >=25 vs. BMI<25	0.52	(0.18, 1.51)	0.229
Never Smoker vs. others	0.97	(0.38, 2.47)	0.948
ECOG PS=0 vs. 1/2/3/4	1.03	(0.37, 2.83)	0.962
High Throbogenic Tumor yes vs. no	0.60	(0.22, 1.59)	0.300
Indwelling central venous yes vs. no	3.11	(1.10, 8.82)	0.033
Platelet < 150K vs. >=150K	1.86	(0.62, 5.55)	0.265
Alubmin >=3.5mg/dL vs. <3.5mg/dL	0.72	(0.24, 2.12)	0.545
Metastasis yes vs. no	0.39	(0.13, 1.19)	0.098
Bevacizmab use yes vs. no	0.20	(0.05, 0.79)	0.022
Index VTE was PE vs non PE	1.56	(0.61, 3.97)	0.349

eTable 6. Association Between the Treatment Selection and the Baseline Characteristics With and Without Adjustment by the Inverse Probability Weighting by the Propensity Scores in the Preference Cohort

	Unadjusted difference		Adjusted difference	
Baseline characteristics	Odds Ratio	P-value	Odds Ratio	P-value
Age 65 or older vs. others	0.80	0.596	0.92	0.742
Female vs. Male	0.61	0.235	0.99	0.967
White vs. Non-White	1.61	0.346	1.14	0.665
Collage grad or higher vs. others	1.19	0.675	1.17	0.534
BMI >=25 vs. BMI<25	0.85	0.707	0.76	0.316
Never Smoker vs. others	1.33	0.490	0.81	0.402
ECOG PS=0 vs. 1/2/3/4	1.12	0.781	0.96	0.875
High Throbogenic Tumor yes vs. no	0.84	0.685	1.26	0.391
Indwelling central venous yes vs. no	1.49	0.338	1.35	0.219
Platelet < 150K vs. >=150K	1.71	0.288	1.01	0.960
Alubmin >=3.5mg/dL vs. <3.5mg/dL	0.99	0.985	0.88	0.619
Metastasis yes vs. no	0.45	0.095	1.05	0.856
Bevacizmab use yes vs. no	0.37	0.081	0.94	0.870
Index VTE was PE vs non PE	1.30	0.523	0.96	0.873
Index VTE was detected by symptom or physical findings vs. others	1.21	0.652	1.49	0.116