Supplemental material

Supplementary table 1. ICD-10 codes used to identify the outcomes of the study

Main outcome	Secondary outcome	ICD-10 code
	Pulmonary embolism (PE)	I26, I26.0, I26.9
Thromboembolic events (TEE)	Deep vein thrombosis (DVT)	G08, I67.6, I80, I80.0, I80.1, I80.2, I80.3, I80.8, I80.9, I81, I82, I82.0, I82.1, I82.2, I82.3, I82.8, I82.9, O22.2, O22.3, O22.5, O87.0, O87.1, O87.3
Cardiovascular events (CVE)	Coronary artery disease (CAD)	I20, I20.0, I20.1, I20.8, I20.9, I21, I21.0, I21.1, I21.2, I21.3, I21.4, I21.9, I22, I22.0, I22.1, I22.8, I22.9, I23, I23.0, I23.1, I23.2, I23.3, I23.4, I23.5, I23.6, I23.8, I24, I24.0, I24.1, I24.8, I24.9, I25, I25.0, I25.1, I25.2, I25.3, I25.4, I25.5, I25.6, I25.8, I25.9, Z95.1
	Cerebrovascular diseases (CVD)	I67.0, I67.1, I67.2, I67.3, I67.4, I67.5, I67.6, I67.7, G46, G46.0, G46.1, G46.2, G46.3, G46.4, G46.5, G46.6, G46.7, G46.8

Supplementary Table 2. Baseline characteristics of candidates using all TAM patients (including ≤55 years all).

Variable	AI N=18,455	Total TAM N=9,537
Median Age (years) [Q1;Q3]	67.0 [59.0;77.0]	49.0 [43.0;61.0]
Mean BMI (kg/m2) ± (SD)	29.7 (5.36)	28.3 (5.53)
Missing, *n* (%)	13,555 (73.45)	7,768 (81.45)
QMEDEA deprivation index, *n* (%):		
Rural population	3,462 (20.3)	1,699 (18.9)
Urban area #1	3,498 (20.5)	1,748 (19.5)
Urban area #2	2,960 (17.4)	1,559 (17.4)
Urban area #3	2,692 (15.8)	1,451 (16.2)
Urban area #4	2,399 (14.1)	1,334 (14.9)
Urban area #5	2,012 (11.8)	1,181 (13.2)
Missing, *n* (% of total)	1,432 (7.76)	565 (5.92)
Charlson co-morbidity index, *n* (%):		
0	2,315 (12.5)	1,062 (11.1)
1	704 (3.81)	171 (1.79)
2	9,840 (53.3)	6,797 (71.3)
3	3,553 (19.3)	1,073 (11.3)
>=4	2,043 (11.1)	434 (4.55)
Smoking status, *n* (%):		
Never smokers	10,269 (81.4)	3,572 (60.7)
Current smokers	1,343 (10.7)	1,527 (25.9)
Ex-smokers (quit >1 year)	997 (7.9)	788 (13.4)
Missing, *n* (% of total)	5,846 (31.68)	3,650 (38.27)
Alcoholism, *n* (%):		
None/Low	2,410 (85.6)	825 (78.3)
Moderate	390 (13.8)	222 (21.1)
High/Alcoholic	16 (0.06)	6 (0.6)
Missing, *n* (% of total)	15,639 (84.74)	8,484 (88.96)
Antiplatelet drug users	1,720 (9.32)	348 (3.65)
Anticoagulant drug users	544 (2.95)	75 (0.79)
Statin drug users	3,518 (19.1)	672 (7.05)
Previous TEE history	496 (2.69)	84 (0.88)
Previous CVE history	693 (3.76)	133 (1.39)

All patients' analysis, non-accounting for postmenopausal status. Abbreviations: AI, aromatase inhibitors; TAM, tamoxifen; BMI, body mass index; Q, quartile; QMEDEA, quintile MEDEA deprivation index; TEE, thromboembolic event; CVE, cerebrovascular event.

Supplementary Table 3. Thromboembolic, cardiovascular and mortality risk of AI treatment compared with TAM treatment (including all TAM users).

a. Hazard risk estimates

Outcome	Number of events		Unadjusted HR (95%CI)	Adjusted HR (95%CI)
TEEs	TAM	107	1.44 (1.16 to 1.79)	0.89 (0.71 to 1.14)
	AI	345		
CVEs	TAM	38	3.08 (2.19 to 4.33)	1.51 (1.06 to 2.15)
	AI	271		
Mortality	TAM	939	1.66 (1.54 to 1.78)	0.80 (0.74 to 0.87)
	AI	3,644		

b. Competing risk estimates

Outcome	Number of events		Unadjusted SHR (95%CI)	Adjusted SHR (95%CI)
TEEs	TAM	107	1.40 (1.13 to 1.75)	0.99 (0.78 to 1.26)
	AI	345		
CVEs	TAM	38	3.00 (2.14 to 4.22)	1.96 (1.37 to 2.81)
	AI	271		

In all patients' analysis, non-accounting for postmenopausal status, AI participants were 18,455 and TAM participants 9,537. Adjusted results were obtained using continuous Propensity

Score estimates. Abbreviations: HR, hazard ratio; SHR, subdistribution hazard ratio; CI, confidence interval; TEEs, thromboembolic events; CVEs, cardiovascular events.

Supplementary Table 4. Risk of PE, DVT, CAD and CVD of AI treatment compared with TAM treatment (including all TAM users).

a. Hazard ratio estimates

Outcome	Subtype	Number of events		Unadjusted HR (95%CI)	Adjusted HR (95%CI)
TEEs	PE	TAM	13	3.24 (1.81 to 5.79)	1.80 (0.98 to 3.30)
		AI	93		
	DVT	TAM	94	1.44 (1.16 to 1.79)	0.79 (0.61 to 1.04)
		AI	252		
CVEs	CAD	TAM	37	3.08 (2.19 to 4.34)	1.49 (1.04 to 2.13)
		AI	260		
	CVD	TAM	1	3.08 (2.18 to 4.36)	2.44 (0.30 to 20.07)
		AI	11		

b. Competing risk estimates

Outcome	Subtype	Number of events		Unadjusted SHR (95%CI)	Adjusted SHR (95%CI)
TEEs	PE	TAM	13	3.17 (1.78 to 5.68)	2.13 (1.16 to 3.91)
		AI	93		

DVT	TAM	94	1.16 (0.92 to 1.48)	0.88 (0.68 to 1.15)
	AI	252		
CVEs	CAD	TAM	37	2.96 (2.10 to 4.18)	1.93 (1.33 to 2.78)
		AI	260		
	CVD	TAM	1	4.63 (0.60 to 35.97)	2.93 (0.35 to 24.24)
		AI	11		

In all patients' analysis, non-accounting for postmenopausal status, AI participants were 18,455 and TAM participants 9,537. Adjusted results were obtained using continuous Propensity Score estimates. Abbreviations: HR, hazard ratio; SHR, subdistribution hazard ratio; CI, confidence interval; TEEs, thromboembolic events; PE, pulmonary embolism; DVT, deep vein thrombosis, phlebitis and thrombophlebitis; CVEs, cardiovascular events; CAD, coronary artery disease; CVD, cerebrovascular diseases, including stroke and intracerebral hemorrhage.

Supplementary Table 5. Risk of thromboembolic and cardiovascular events of AI treatment compared with TAM treatment (including all TAM users) using stabilized Inverse Probability Weighting adjustment.

Outcome and subtypes	Number of events		Stabilized IPW HR (95%CI)
TEEs	TAM	107	0.83 (0.61 to 1.14)
	AI	345	
PE	TAM	13	0.98 (0.44 to 2.20)
	AI	93	

DVT	TAM	94	0.79 (0.57 to 1.10)
	AI	252	
CVEs	TAM	38	0.87 (0. 56 to 1.38)
	AI	271	
CAD	TAM	37	0.85 (0.53 to 1.39)
	AI	260	
CVD	TAM	1	0.91 (0.11 to 7.62)
	AI	11	
Mortality	TAM	939	0.48 (0.44 to 0.53)
	AI	3,644	

In all patients' analysis, non-accounting for postmenopausal status, AI participants were 18,455 and TAM participants 9,537. Abbreviations: IPW HR, Inverse probability weighting hazard ratio; CI, confidence interval; TEEs, thromboembolic events; PE, pulmonary embolism; DVT, deep vein thrombosis, phlebitis and thrombophlebitis; CVEs, cardiovascular events; CAD, coronary artery disease; CVD, cerebrovascular diseases, including stroke and intracerebral hemorrhage.