

Epidemiological study regarding the incidence of venous thromboembolism in patients after cancer remission

Miki Imura¹, Jun Katada¹, Taro Shiga²

¹Medical Affairs, Internal Medicine, Pfizer Biopharmaceuticals Group, Pfizer Japan Inc., Tokyo, Japan

²Department of Onco-Cardiology/Cardiovascular Medicine, The Cancer Institute Hospital of Japanese Foundation for Cancer Research, Tokyo, Japan

Corresponding author: Miki Imura

Medical Affairs, Internal Medicine,
Pfizer Biopharmaceuticals Group, Pfizer Japan Inc.
3-22-7, Yoyogi, Shibuya-ku, Tokyo 151-8589 Japan
Phone: +81-80-5001-3070, Fax: +81-3-5309-9198
Email: miki.imura@pfizer.com

Supplementary Table 1**Table S1. EphMRA ATC code used for the definition of medications**

Medications	EphMRA ATC
Alkylating agents	L01A, trabectedin
Anti-metabolites	L01B
Microtubule inhibitors	L01C1,2
Cytotoxic antibiotics	L01C3,4, L01D, sobuzoxane
PK inhibitor	L01H
Monoclonal antibodies	L01G1,2,3,4,5, satuximab, inotuzumab ozogamicin, Lipilimumab (genetic modification), elotuzumab, gemtuzumab, daratumumab, blinatumomab, brentuximab vedotin, polatuzumab vedotin, mogamulizumab
Platinum agents	L01F0
Other anti-cancer drugs	L01J, L01X3,4,5,8, procarbazine, L-asparaginase, hydroxycarbamide, estramustine, phosphate arsenic trioxide, venetoclax, tamibarotene, eribulin, forodesin
Hormones	L02A1,2,3, medroxyprogesterone
Hormone antagonist	L02B

PK, protein kinase

Supplementary Table 2**Table S2. International Classification of Disease codes, version 10, used for the definition of comorbidities**

Diseases	ICD-10 codes
Malignant tumor	
Oral/esophagus	C0, C10, C11, C12, C13, C14, C15, C30, C31, C32
Stomach	C16
Intestine	C17, C18, C19, C20, C21
Liver	C22, C23, C24
Pancreas	C25
Lung	C33, C34
Thymus/Heart	C37, C38
Bone/Joint	C40, C41
Skin	C43, C44, C45, C46, C47, C48, C49
Breast	C50
Female reproductive	C51, C52, C53, C54, C55, C56, C57, C58
Male reproductive	C60, C61, C62, C63
Kidney	C64, C65, C66, C67, C68
CNS	C69, C70, C71, C72
Endocrine	C73, C74, C75
Lymph/blood	C81, C82, C83, C84, C85, C86, C87, C88, C90, C91, C92, C94, C95, C96
Comorbidities	
Sepsis	A021, A207, A227, A267, A327, A40, A41, A427, B377
Coagulopathy	D65, C66, C67, C68, C69
Diabetes mellitus	E11, E12, E13, E14
Diabetes mellitus with complications	E11, E12, E13, E14, E25, E27
Dyslipidemia	E78
Stress	F43
Sleep disorder	G47
Hypertension	I10, I11, I12, I13, I14, I15
Angina	I20
Previous myocardial infarction	I21, I22, I23, I252
Pulmonary embolism	I26
Deep vein thrombosis	I80, I81, I82, O222, O223, O225, O870, O871, O887
Pericarditis	I30, I31, I32, I33, I38, I398
Valvular disease	I05, I06, I07, I08, I34, I35, I36, I37, I390, I391, I392, I393, I394
Cardiomyopathy	I40, I41, I42, I43, I012, I090, I255, I514
Atrial fibrillation	I480, I481, I482, I489
Conduction failure	I44, I45, I47, I483, I484, I49
Heart failure	I50, I110, I130, I132
Stroke	
Intracerebral hemorrhage	I60, I61, I62, I690, I691, I692
Ischemic stroke	I63, I693
Atheroma	I70
Peripheral thrombosis	I742, I743, I744, I745, I746, I747, I748, I749, I80, I82
Peptic ulcer	K25, K26, K27, K28
Gastritis	K29, K30

Mild liver disease	B18, K700, K703, K709, K713, K714, K715, K716, K73, K74, K760, K762, K763, K764, K768, K769, Z955
Moderate/Severe liver	I850, I859, I864, I982, K704, K711, K721, K729, K765, K766, K767
Rheumatic disease	M05, M06, M315, M32, M33, M34, M351, M353, M360
Renal disease	I120, I131, N02, N03, N04, N05, N06, N07, N18, N19, N250, Z490, Z491, Z492, Z940, Z992

ICD, International Classification of Disease; CNS, central nervous system

Supplementary Table 3**Table S3. Definitions of anticancer treatment for malignant tumor**

Class	Procedure
Cancer surgery	tumor (surgery, extirpation excision) excision decollement extirpation
Stem cell transplant	Stem cell transplant, with lymphadenectomy dissection dissection with dissection dissection Concomitant application
Radiation etc.	Radio wave Microwave Photodynamics Electromagnetic wave Radiation source treatment Laser Particle beam therapy Extracorporeal irradiation Linear accelerator Gamma knife
Topical administration	Local continuous injection Anti-malignant tumor agent
Outpatient chemotherapy	Outpatient chemotherapy
Cancer pain	Cancer pain management fee
Cancer rehabilitation	Cancer patient rehabilitation fee

Supplementary Table 4**Table S4. Patient characteristics**

Variables	Entire cohort (N=638,908)	Patients without VTE (N=633,375)	Patients with VTE (N=5,533) (PE: 779, DVT: 5,084)	P
Demographics				
Male	328,426 (51.4)	325,798 (51.4)	2,628 (47.5)	<0.001
Age (years)	67.8±13.4	67.8±13.4	70.1±12.5	<0.001
Comorbidity				
Sepsis	8,471 (1.3)	8,343 (1.3)	128 (2.3)	<0.001
Coagulopathy	26,069 (4.1)	25,630 (4.0)	439 (7.9)	<0.001
Diabetes mellitus	142,749 (22.3)	141,090 (22.3)	1,659 (30.0)	<0.001
Diabetes mellitus+	19,578 (3.1)	19,270 (3.0)	308 (5.6)	<0.001
Dyslipidemia	103,527 (16.2)	102,349 (16.2)	1,178 (21.3)	<0.001
Sleep disorder	102,970 (16.1)	101,802 (16.1)	1,168 (21.1)	<0.001
Hypertension	200,755 (31.4)	198,414 (31.3)	2,341 (42.3)	<0.001
Angina	48,515 (7.6)	47,798 (7.5)	717 (13.0)	<0.001
Previous myocardial infarction	10,959 (1.7)	10,799 (1.7)	160 (2.9)	<0.001
Pulmonary embolism	1,379 (0.2)	1,288 (0.2)	91 (1.6)	<0.001
Deep vein thrombosis	15,881 (2.5)	15,218 (2.4)	663 (12.0)	<0.001
Pericarditis	5,412 (0.8)	5,312 (0.8)	100 (1.8)	<0.001
Valvular disease	30,282 (4.7)	29,887 (4.7)	395 (7.1)	<0.001
Cardiomyopathy	2,871 (0.4)	2,821 (0.4)	50 (0.9)	<0.001
Atrial fibrillation	15,423 (2.4)	15,186 (2.4)	237 (4.3)	<0.001

Conduction failure	36,455 (5.7)	36,029 (5.7)	426 (7.7)	<0.001
Heart failure	45,323 (7.1)	44,551 (7.0)	772 (14.0)	<0.001
Stroke	34,164 (5.3)	33,751 (5.3)	413 (7.5)	<0.001
Intracerebral hemorrhage	4,342 (0.7)	4,276 (0.7)	66 (1.2)	<0.001
Ischemic stroke	30,731 (4.8)	30,366 (4.8)	365 (6.6)	<0.001
Atheroma	11,870 (1.9)	11,655 (1.8)	215 (3.9)	<0.001
Peripheral thrombosis	20,370 (3.2)	19,666 (3.1)	704 (12.7)	<0.001
Peptic ulcer	142,027 (22.2)	140,565 (22.2)	1,462 (26.4)	<0.001
Gastritis	146,657 (23.0)	145,144 (22.9)	1,513 (27.3)	<0.001
Mild liver	74112 (11.6)	73178 (11.6)	934 (16.9)	<0.001
Moderate/Severe liver	6,997 (1.1)	6,814 (1.1)	183 (3.3)	<0.001
Rheumatic Disease	9,471 (1.5)	9,289 (1.5)	182 (3.3)	<0.001
Renal disease	22,128 (3.5)	21,761 (3.4)	367 (6.6)	<0.001

Medications

Heparin	196,882 (30.8)	194,637 (30.7)	2,245 (40.6)	<0.001
Low-molecular-weight heparin	37,734 (5.9)	37,279 (5.9)	455 (8.2)	<0.001
Fondaparinux	2,109 (0.3)	2,067 (0.3)	42 (0.8)	<0.001
Anti-platelet drugs	58,565 (9.2)	57,829 (9.1)	736 (13.3)	<0.001
Thrombolytics	533 (0.1)	520 (0.1)	13 (0.2)	<0.001
Warfarin	1768 (0.3)	1687 (0.3)	81 (1.5)	<0.001
Thrombin inhibitors	717 (0.1)	701 (0.1)	16 (0.3)	<0.001
FXa inhibitors	3,723 (0.6)	3,574 (0.6)	149 (2.7)	<0.001
other anticoagulants	3,479 (0.5)	3,422 (0.5)	57 (1.0)	<0.001

Female hormone	5,964 (0.9)	5,886 (0.9)	78 (1.4)	<0.001
NSAIDs	366,482 (57.4)	363,094 (57.3)	3,388 (61.2)	<0.001
Anti-arrhythmic drugs	79,097 (12.4)	78,222 (12.4)	875 (15.8)	<0.001
Digitalis	2,892 (0.5)	2,843 (0.4)	49 (0.9)	<0.001

FXa, factor Xa; NSAIDs, nonsteroidal anti-inflammatory drugs; VTE, venous thromboembolism; DVT, deep venous thrombosis

“Diabetes mellitus +” was identified as diabetic with complications (E110, E111, E112, E113, E114, E115, E116, E117, E130, E131, E132, E133, E134, E135, E136, E137, E141, E142, E143, E144, E145, E146)

Female hormone; G03C0, G03D0, G03E0, G03F0, G03J0,

Hormone antagonist; L02B