Antithrombotic Efficacy and Safety of Dabigatran Etexilate

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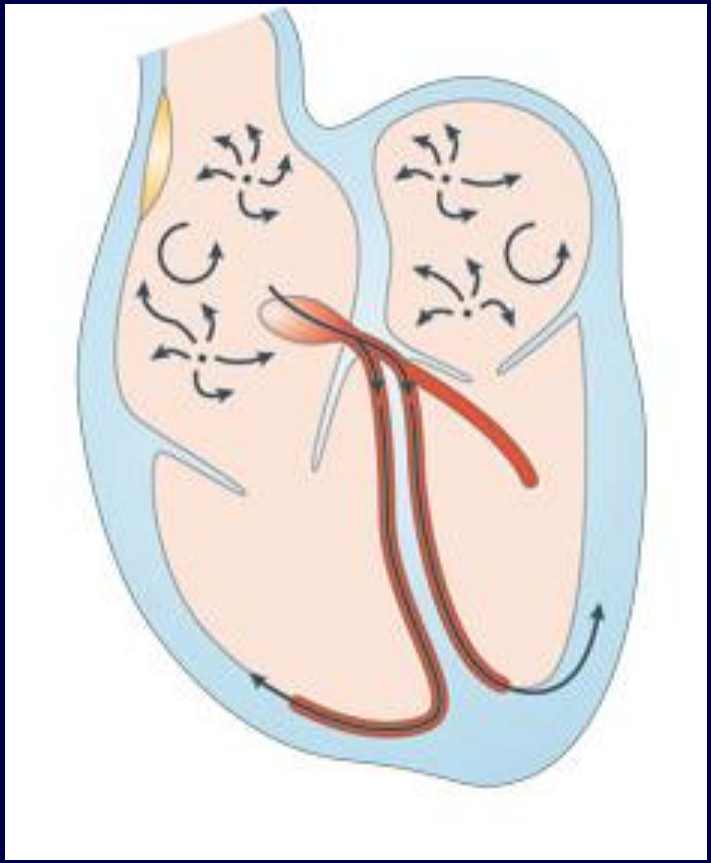
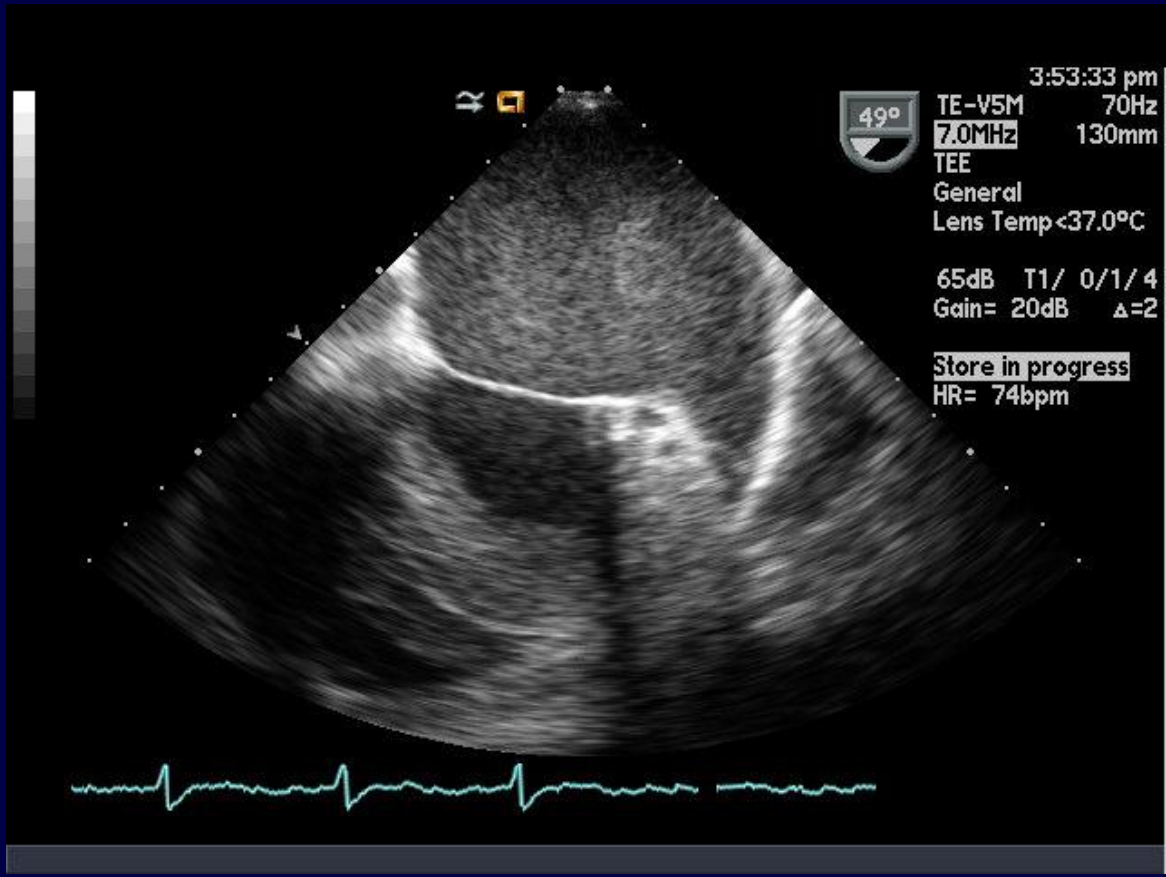
Atrial Fibrillation

Risk of Stroke





CHA_2DS_2-VASc Score

2010 ESC Guideline

$CHADS_2$ Score (6)

- CHF (1)
- Hypertension (1)
- Age > 75 (1)
- DM (1)
- Stroke/ TIA (2)

$CHADS_2$ Score ≥2 : OAC
$CHADS_2$ Score =1 : OAC = ASA

CHA_2DS_2–VASc Score (9)

- CHF (1)
- Hypertension (1)
- Age > 75 (2)
- DM (1)
- Stroke/ TIA (2)
- Vascular Disease (1)
- Age 65~75 (1)
- Female Sex (1)

CHA_2DS_2 VASc Score ≥2 : OAC
CHA_2DS_2 VASc Score =1 : OAC ≥ ASA

Camm AJ et al. Eur Heart J. 2010;31(19):2369-242

HAS-BLED Score (Bleeding Risk)

2010 ESC Guideline

Camm AJ et al. Eur Heart J. 2010;31(19):2369-2429.

Table 6: Clinical characteristics comprising the HAS-BLED bleeding risk score

Letter	Clinical characteristic*	Points awarded
H	Hypertension	1
A	Abnormal renal and liver function (1 point each)	1 or 2
S	Stroke	1
B	Bleeding	1
L	Labile INRs	1
E	Elderly (e.g. age > 65 years)	1
D	Drugs or alcohol (1 point each)	1 or 2
		Maximum 9 points

HAS-BLED Score ≥ 3:
High risk of bleeding. Regular review is needed. (Class IIa)

CHA_2DS_2-VASc Score

2010 ESC Guideline

$CHADS_2$ Score (6)

• CHF	(1)
• Hypertension	(1)
• Age > 75	(1)
• DM	(1)
• Stroke/ TIA	(2)

$CHADS_2$ Score ≥2 : OAC
$CHADS_2$ Score =1 : OAC = ASA

CHA_2DS_2–VASc Score (9)

• CHF	(1)
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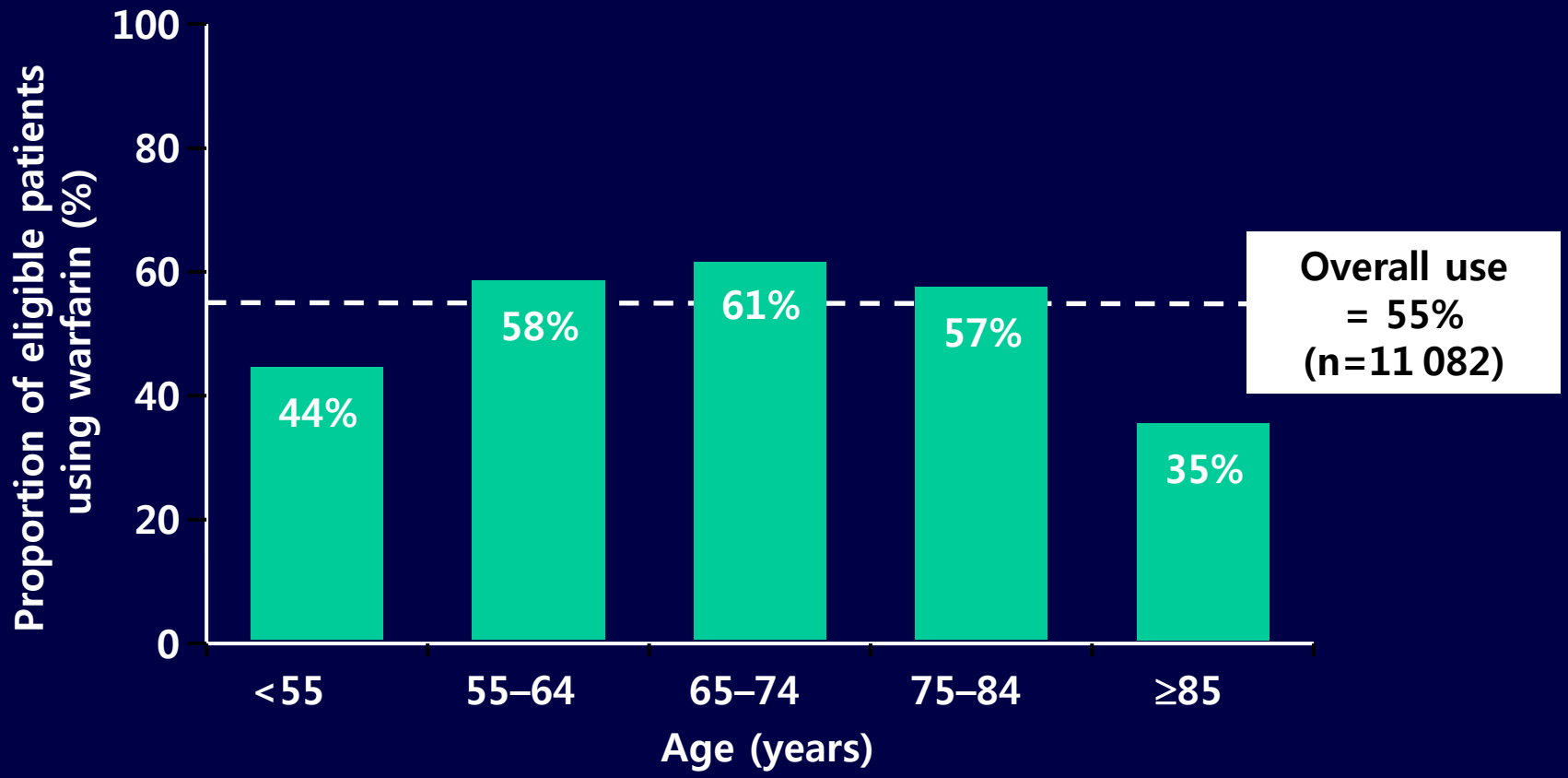
• Vascular Disease	(1)
• Age 65~75	(1)
• Female Sex	(1)

CHA_2DS_2 VASc Score ≥2 : OAC
CHA_2DS_2 VASc Score =1 : OAC ≥ ASA

Camm AJ et al. Eur Heart J. 2010;31(19):2369-242

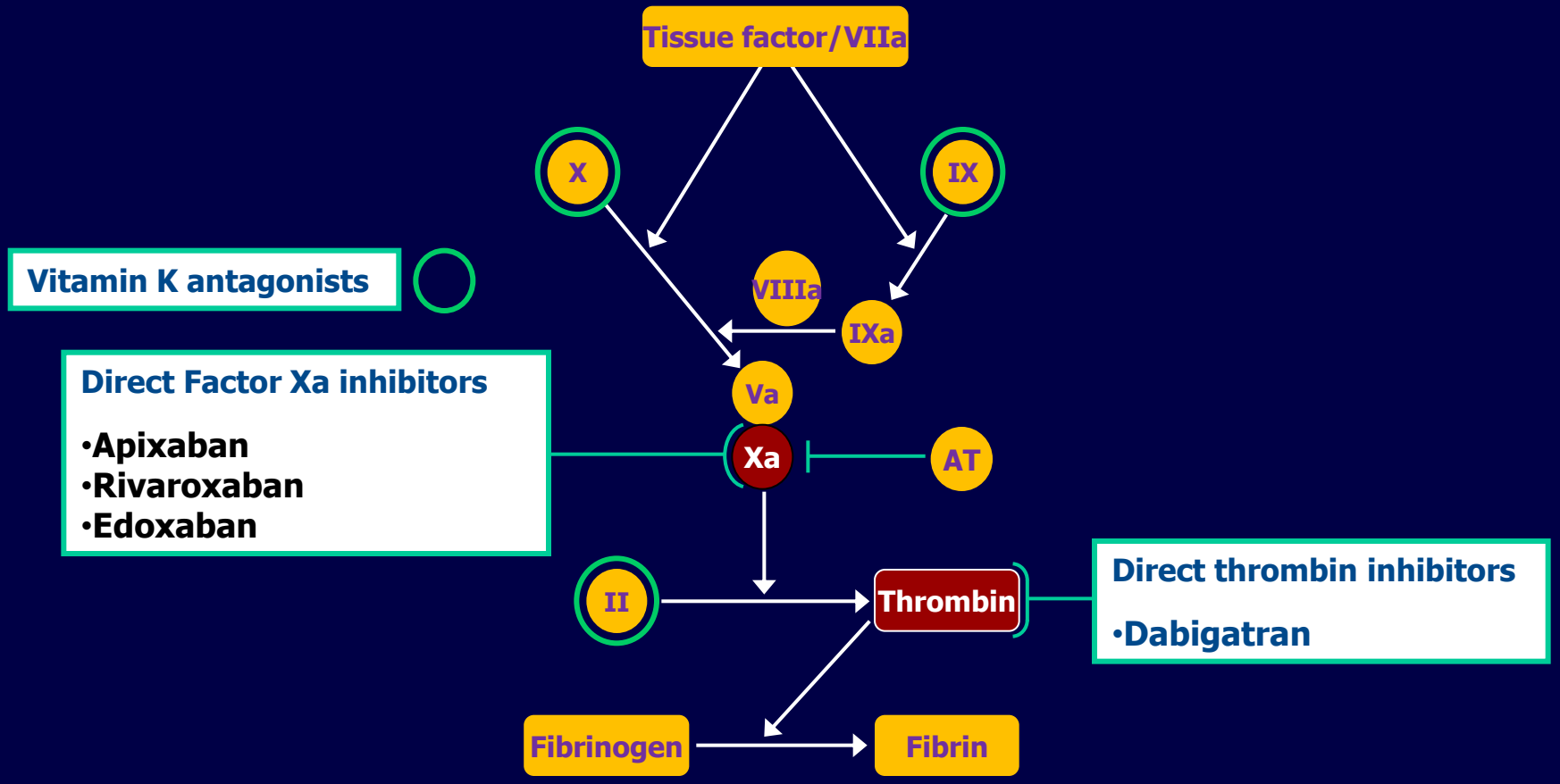
VKAs used in only half of eligible patients with AF



VKA = vitamin K antagonist

Go A et al. Ann Intern Med 1999;131:927-34

Novel agents target specific molecules in the coagulation cascade



Weitz J, Bates S. J Thromb Haemost 2005;3:1843-53; Monroe D, Hoffman M. Arterioscler Thromb Vasc Biol 2006;26:41-8; Crawley J et al. J Thromb Haemost 2007;5 (Suppl 1):95-101

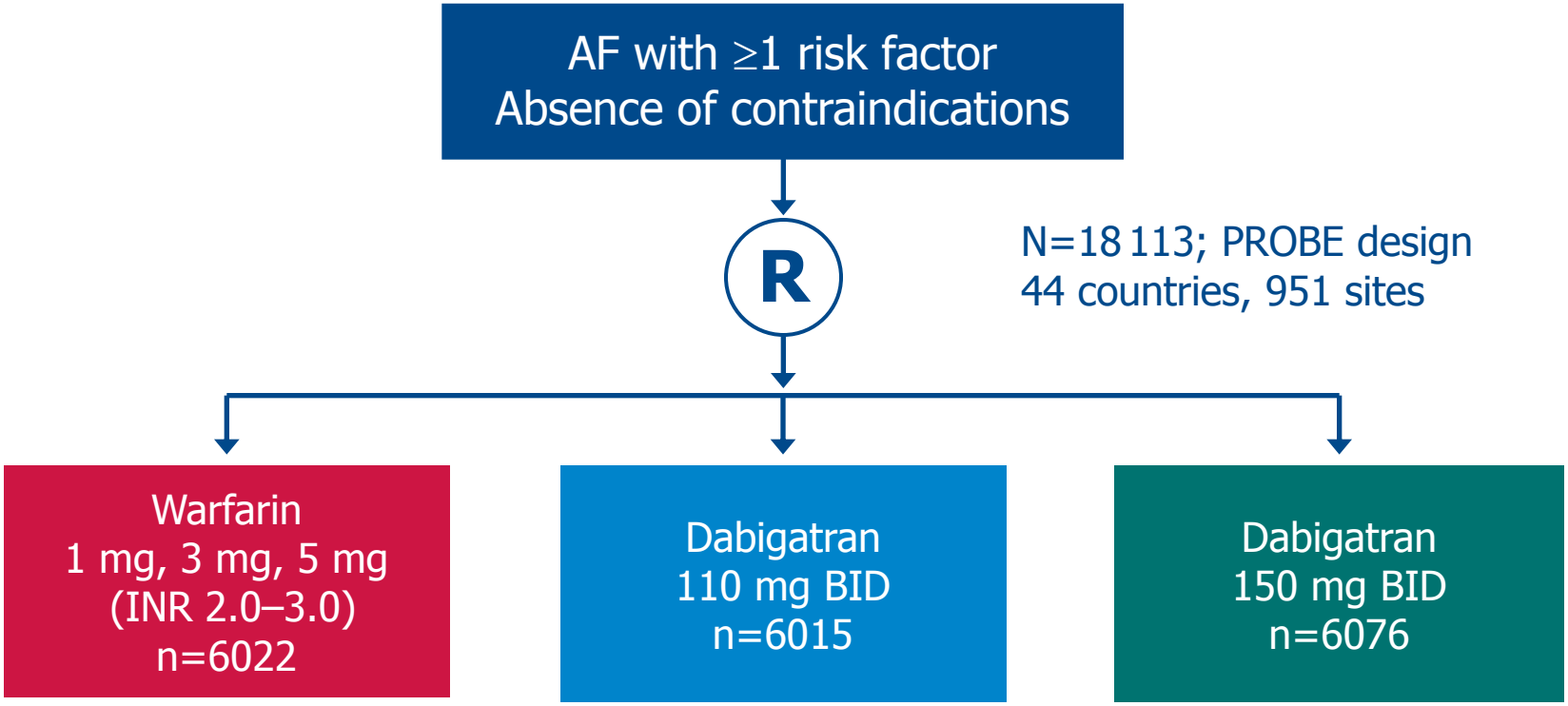
Properties of novel agents for stroke prevention

	Dabigatran	Rivaroxaban	Apixaban
Target	Thrombin	Factor Xa	Factor Xa
Dosing	Fixed, twice daily	Fixed, once daily	Fixed, twice daily
Half-life in hours	12–14	7–13	8–13
Routine monitoring	No	No	No
Renal clearance	**80%**	**66%**	**25%**
Involvement of CYP	No	Yes (CYP3A4)	Yes (CYP3A4)

CYP = cytochrome P450

Adapted from Eriksson B et al. Annu Rev Med 2011;62:41-57

RE-LY®: trial design



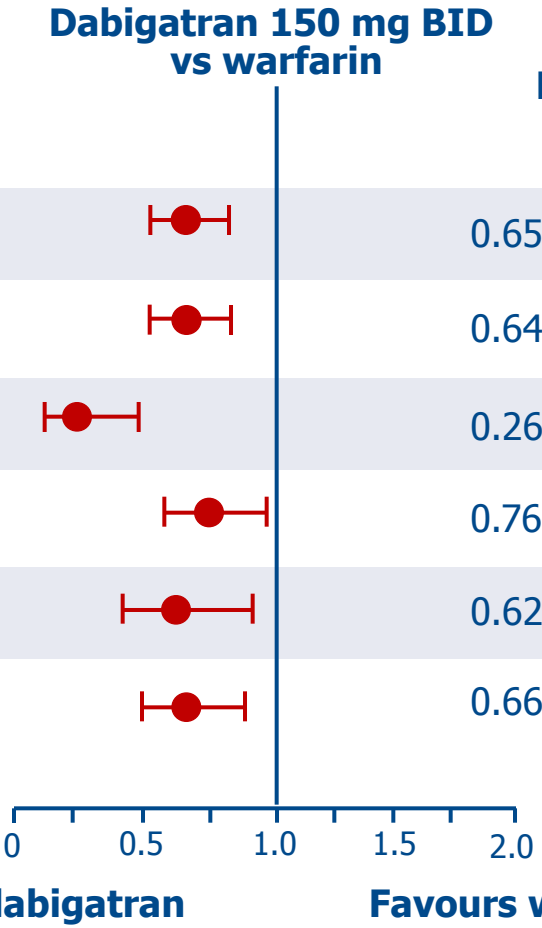
- Primary objective: establish the non-inferiority of dabigatran to warfarin
- Follow-up: minimum of 1 year, maximum of 3 years, median of 2 years

BID = twice daily; INR = international normalized ratio; R = randomization

Ezekowitz MD et al. Am Heart J 2009;157:805–10; Connolly SJ et al. N Engl J Med 2009;361:1139–5

Dabigatran 150 mg BID was superior to warfarin for the prevention of stroke and systemic embolism

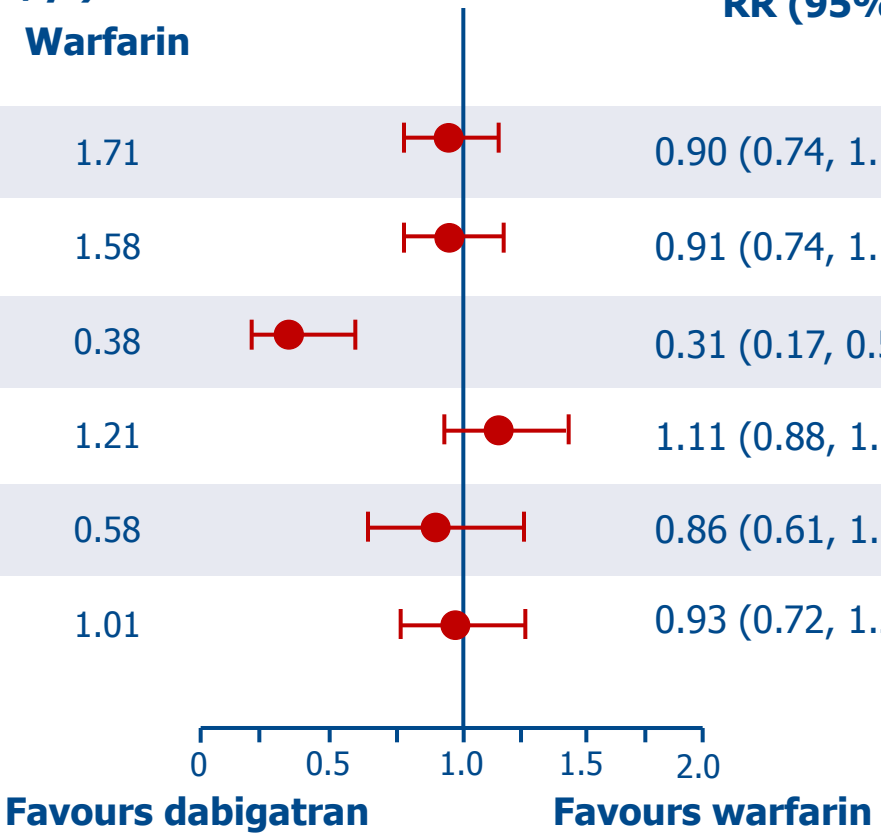
	Rate (%/yr)		RR (95% CI); P value
	Dabigatran	Warfarin	
Stroke or systemic embolism	1.11	1.71	0.65 (0.52, 0.81); P<0.001
Stroke	1.01	1.58	0.64 (0.51, 0.81); P<0.001
Haemorrhagic stroke	0.10	0.38	0.26 (0.14, 0.49); P<0.001
Ischaemic	0.92	1.21	0.76 (0.59, 0.97); P=0.03
Non-disabling stroke	0.37	0.58	0.62 (0.43, 0.91); P=0.01
Disabling or fatal stroke	0.66	1.01	0.66 (0.50, 0.87); P=0.004



- Error bars = 95% CI; BID = twice daily; Intention-to-treat population
- Connolly SJ et al. N Engl J Med 2009;361:1139–51; Connolly SJ et al. N Engl J Med 2010;363:1875–6; Pradaxa® EU SmPC, June 2012

Dabigatran 110 mg BID was non-inferior to warfarin for the prevention of stroke and systemic embolism

	Rate (%/yr)		Dabigatran 110 mg BID vs warfarin
	Dabigatran	Warfarin	RR (95% CI); P value
Stroke or systemic embolism	1.54	1.71	0.90 (0.74, 1.10); P<0.001*
Stroke	1.44	1.58	0.91 (0.74, 1.12); P=0.38
Haemorrhagic stroke	0.12	0.38	0.31 (0.17, 0.56); P<0.001
Ischaemic	1.34	1.21	1.11 (0.88, 1.39); P=0.35
Non-disabling stroke	0.50	0.58	0.86 (0.61, 1.22); P=0.40
Disabling or fatal stroke	0.94	1.01	0.93 (0.72, 1.21); P=0.61



*P value for non-inferiority; Error bars = 95% CI; BID = twice daily; Intention-to-treat population

Connolly SJ et al. N Engl J Med 2009;361:1139–51; Connolly SJ et al. N Engl J Med 2010;363:1875–6; Pradaxa® EU SmPC, June 2012

RE-LY®: bleeding outcomes

Characteristic	Dabigatran 110 mg BID (n=6015)	Dabigatran 150 mg BID (n=6076)	Warfarin (n=6022)	P value D 110 mg vs W	P value D 150 mg vs W
Major bleeding	**2.87**	3.32	**3.57**	**0.003**	0.31
– Life-threatening	**1.24**	1.49	1.85	**<0.001**	**0.03**
– Non-life threatening	1.83	2.06	1.92	0.65	0.39
– Gastrointestinal	1.15	**1.56**	1.07	0.52	**0.001**
Intracranial bleeding	**0.23**	**0.32**	**0.76**	**<0.001**	**<0.001**

Data represent %/year

D = dabigatran; W = warfarin; Intention-to-treat population

Connolly SJ et al. N Engl J Med 2010;363:1875–6

The Long Term Multi-center Extension of Dabigatran Treatment in Patients with Atrial Fibrillation (RELY-ABLE®) study

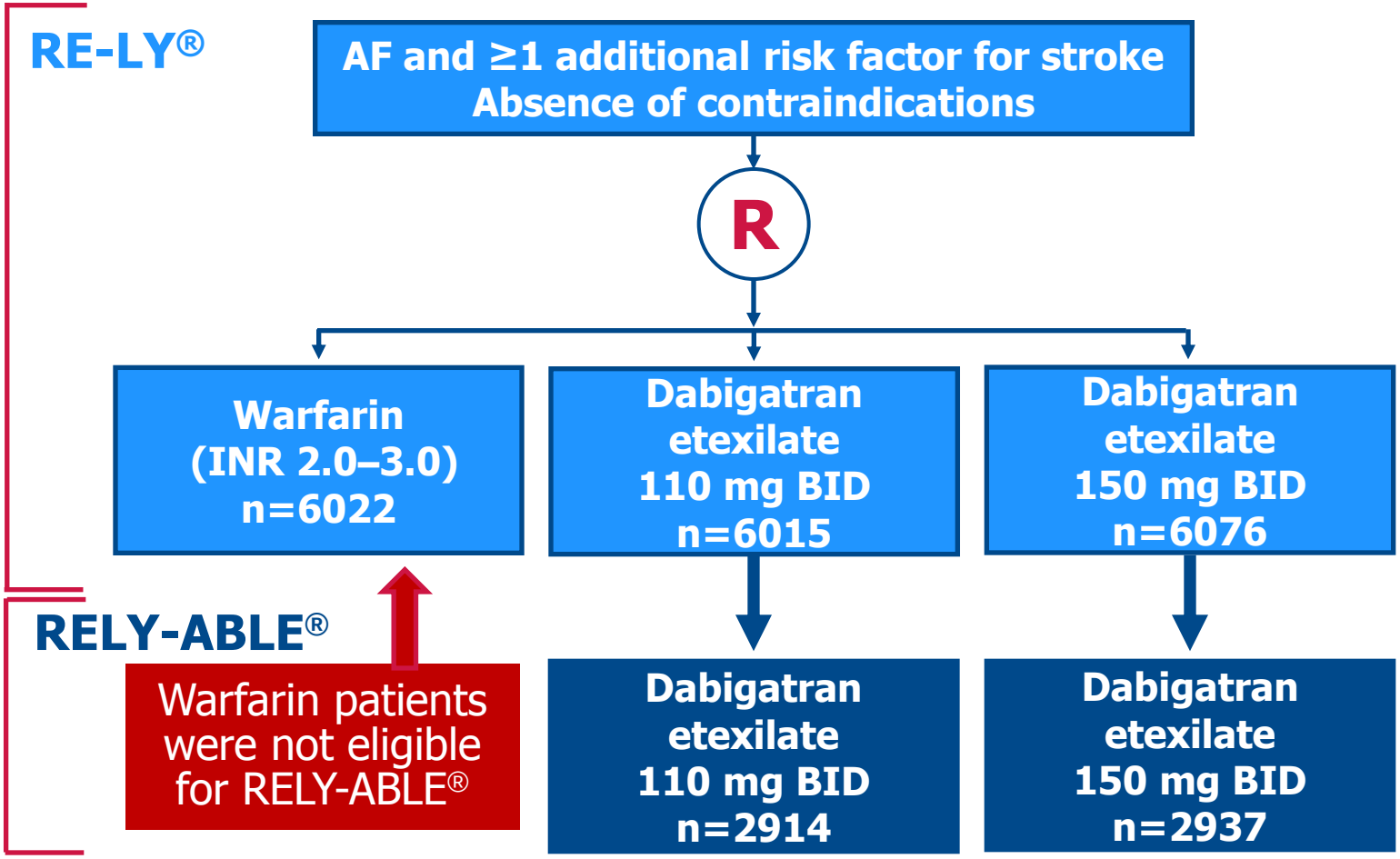
RELY-ABLE® Steering Committee and Investigators

RELY-ABLE® goals and design

- Goals
  - To describe the **long-term efficacy and safety of ongoing Dabigatran therapy following RE-LY®**
- Methods
  - Patients eligible at completion of RE-LY® study if:
    - Alive and still receiving study Dabigatran
    - Being followed at centers participating in RELY-ABLE®
  - Dabigatran blinded dose continued in RELY-ABLE® for 2.3 years
- Analysis
  - Two follow-up periods described
    - RELY-ABLE® (post-RE-LY®)
    - RE-LY® + RELY-ABLE® (beginning of RE-LY® to end of RELY-ABLE®)

Together with RE-LY®, this allows for over 4 years of follow-up in total

RELY-ABLE®: extension of RE-LY®

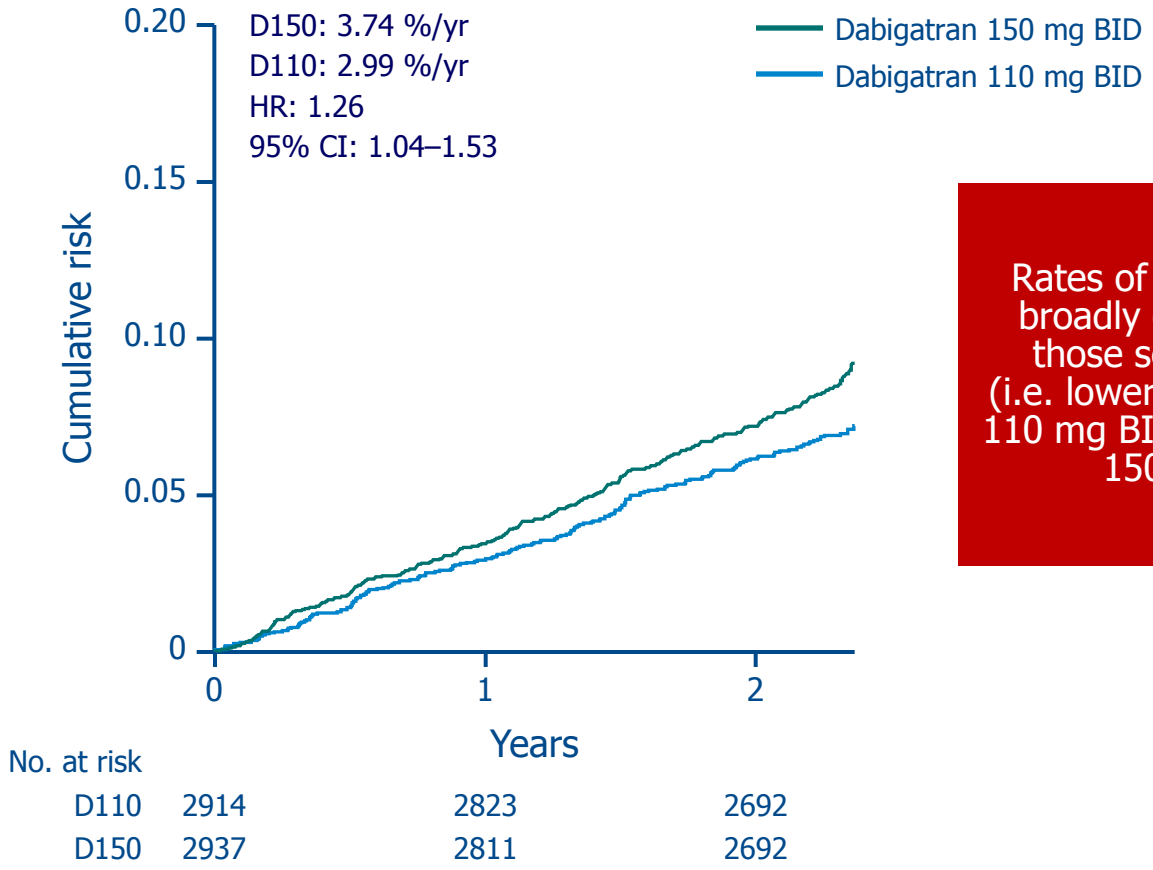


RELY-ABLE® Design: summary

- **First long-term data for a NOAC**
  - Over 4 years of follow-up
- **To assess long-term safety of Dabigatran**
- Points to note:
  - Population not randomized
  - Outcome events not adjudicated
  - Warfarin patients not included
- Dose comparison
  - Highlights the tailored protection that Dabigatran can provide

OAC = oral anticoagulant

Major bleeding: RELY-ABLE®



Rates of major bleeding broadly consistent with those seen in RE-LY® (i.e. lower with Dabigatran 110 mg BID compared with 150 mg BID)

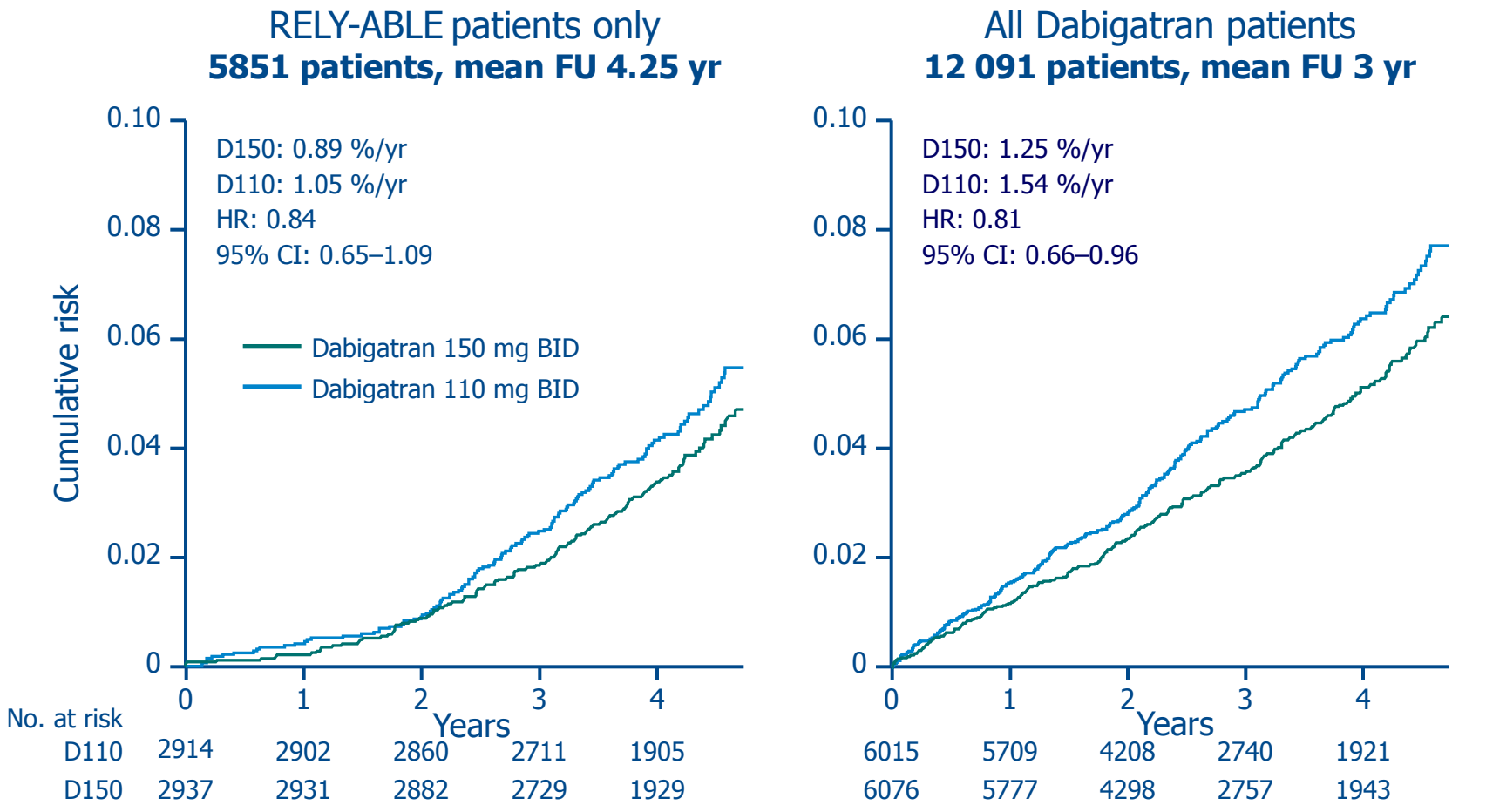
Bleeding events: RELY-ABLE®

Event	RELY-ABLE® only			
	D150 (%/yr)	D110 (%/yr)	HR	95% CI
Major bleeding (W3.6)	3.74	2.99	1.26	1.04–1.53
Life-threatening	1.79	1.57	1.14	0.87–1.49
GI (W1.5)	1.54	1.56	0.99	0.75–1.31
Intra-cranial (W0.8)	0.33	0.25	1.31	0.68–2.51
Extra-cranial	3.43	2.82	1.23	1.01–1.49
Fatal	0.24	0.25	0.94	0.46–1.89
Minor bleeding	9.70	8.19	1.21	1.07–1.36

In contrast to RE-LY®, rates of GI bleeding in RELYABLE® were comparable with both doses of Dabigatran

Rates of ICH were low for both doses as in RE-LY

Stroke/systemic embolism: RE-LY® + RELY-ABLE®



In the secondary analysis of RE-LY® and RELYABLE®, Dabigatran 150 mg BID was associated with a lower rate of stroke and systemic embolism than the 110 mg BID dose

W 1.7%/yr

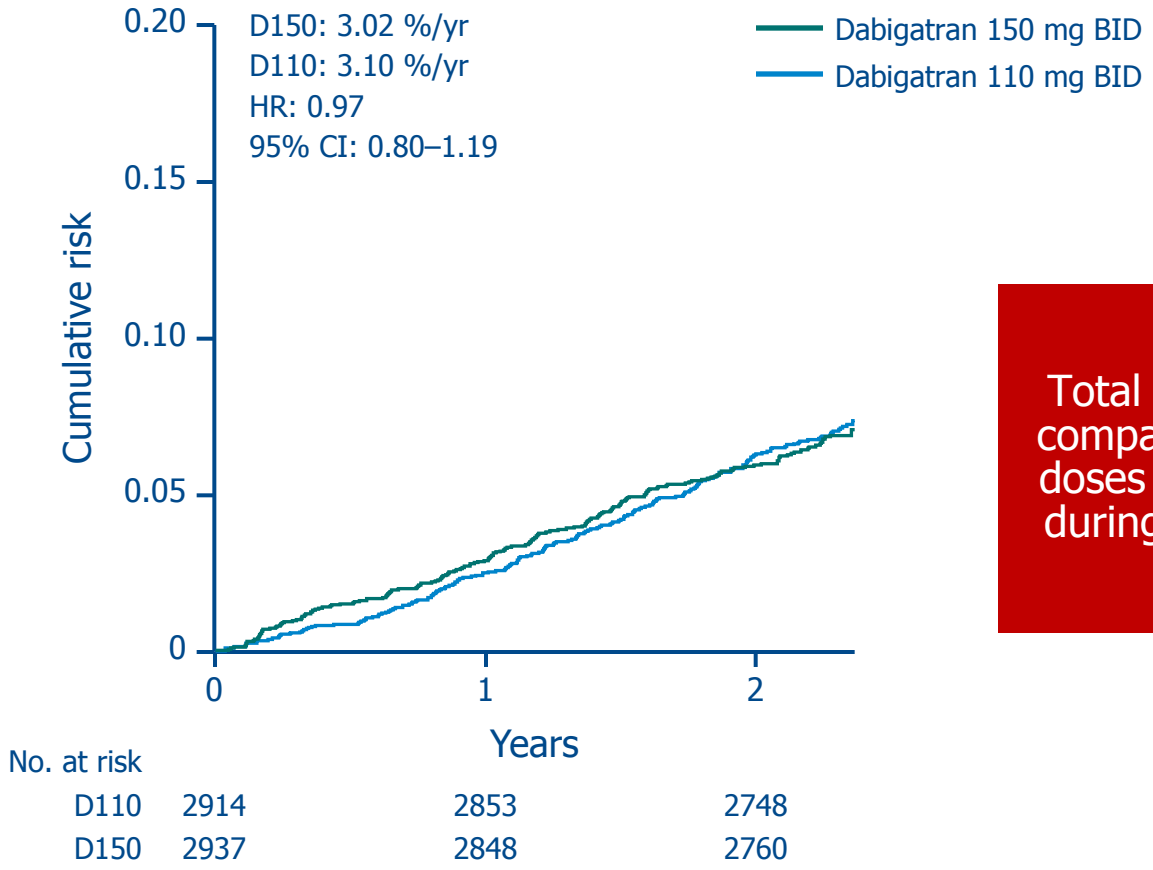
Stroke and ischaemic events: RELY-ABLE®

Event	D150 (%/yr)	D110 (%/yr)	HR	95% CI
Stroke or SEE	1.46	1.60	0.91	0.69–1.20
All stroke	1.24	1.38	0.89	0.66–1.21
Ischaemic (W1.7)	1.15	1.24	0.92	0.67–1.27
Haemorrhagic (W0.8)	0.13	0.14	0.89	0.34–2.30
Myocardial infarction (W0.64)	0.69	0.72	0.96	0.63–1.45
Pulmonary embolism	0.13	0.11	1.14	0.41–3.15

Rates of ischemic stroke were consistent with those in RE-LY® – lower with 150mg BID vs. 110mg BID

Rate of MI was low during RELYABLE® and comparable for both doses of Dabigatran

Total mortality: RELY-ABLE®



Total mortality was comparable for both doses of Dabigatran during RELY-ABLE®

Conclusion

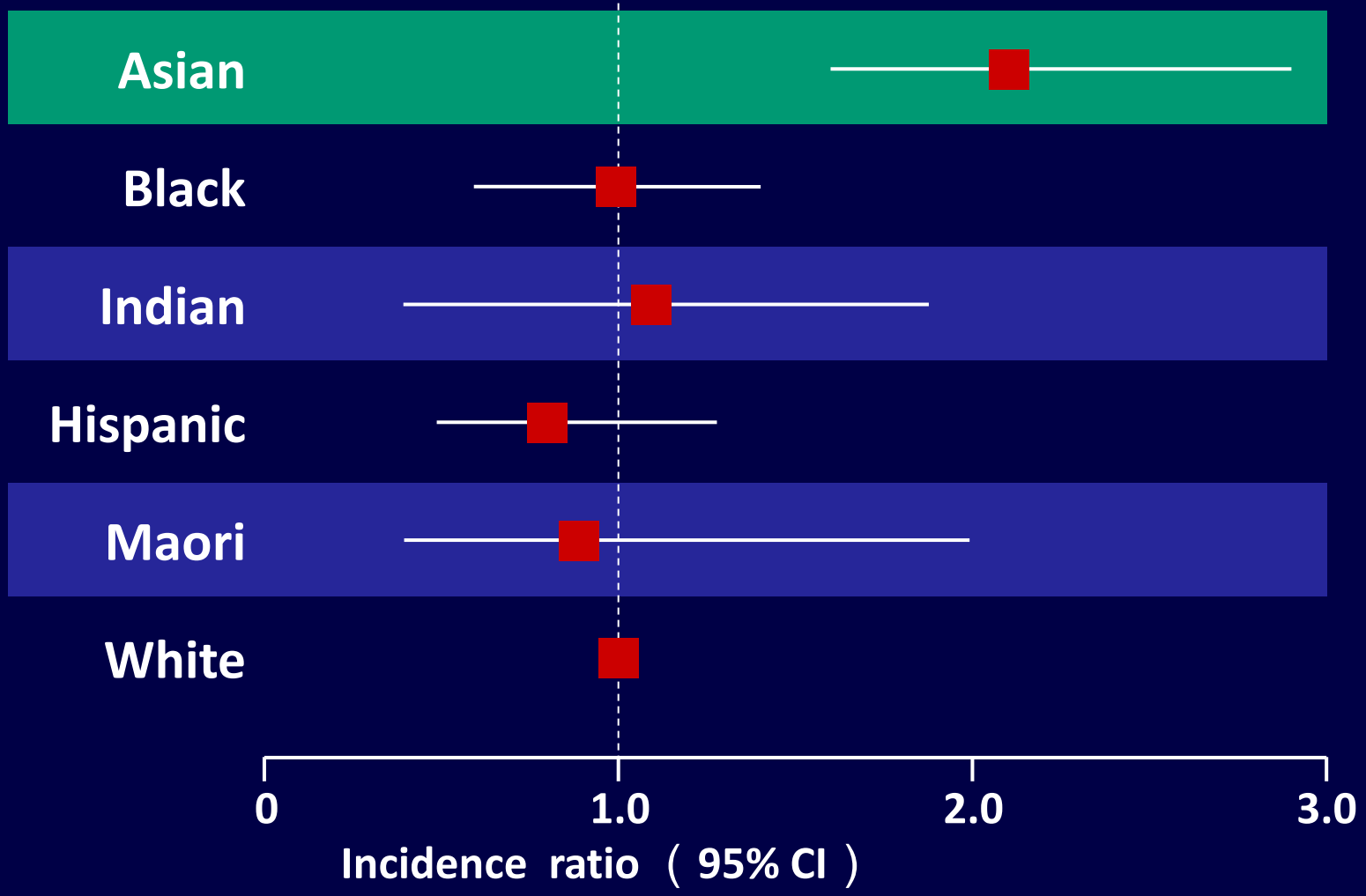
- During 2.3 years of additional treatment after RE-LY® (total mean follow-up 4.3 years), rates of stroke and major bleeding remain low on Dabigatran and are **consistent with those seen during RE-LY®**

- Dabigatran 150 vs. Dabigatran 110
  - Both doses have very low rates of hemorrhagic stroke over 4+ years
  - With Dabigatran 150, there is a lower rate of ischaemic stroke but a higher rate of major bleeding
  - Both doses have similar mortality

Efficacy and Safety of Dabigatran vs. Warfarin in Patients with AF: Analysis in ASIAN Population in RE-LY Trial

Incidence ratios of Cerebral hemorrhage in ethnic groups (Meta-analysis) n=8,145

van Asch CJ, et al.: Lancet Neurol 9, 167-176, 2010

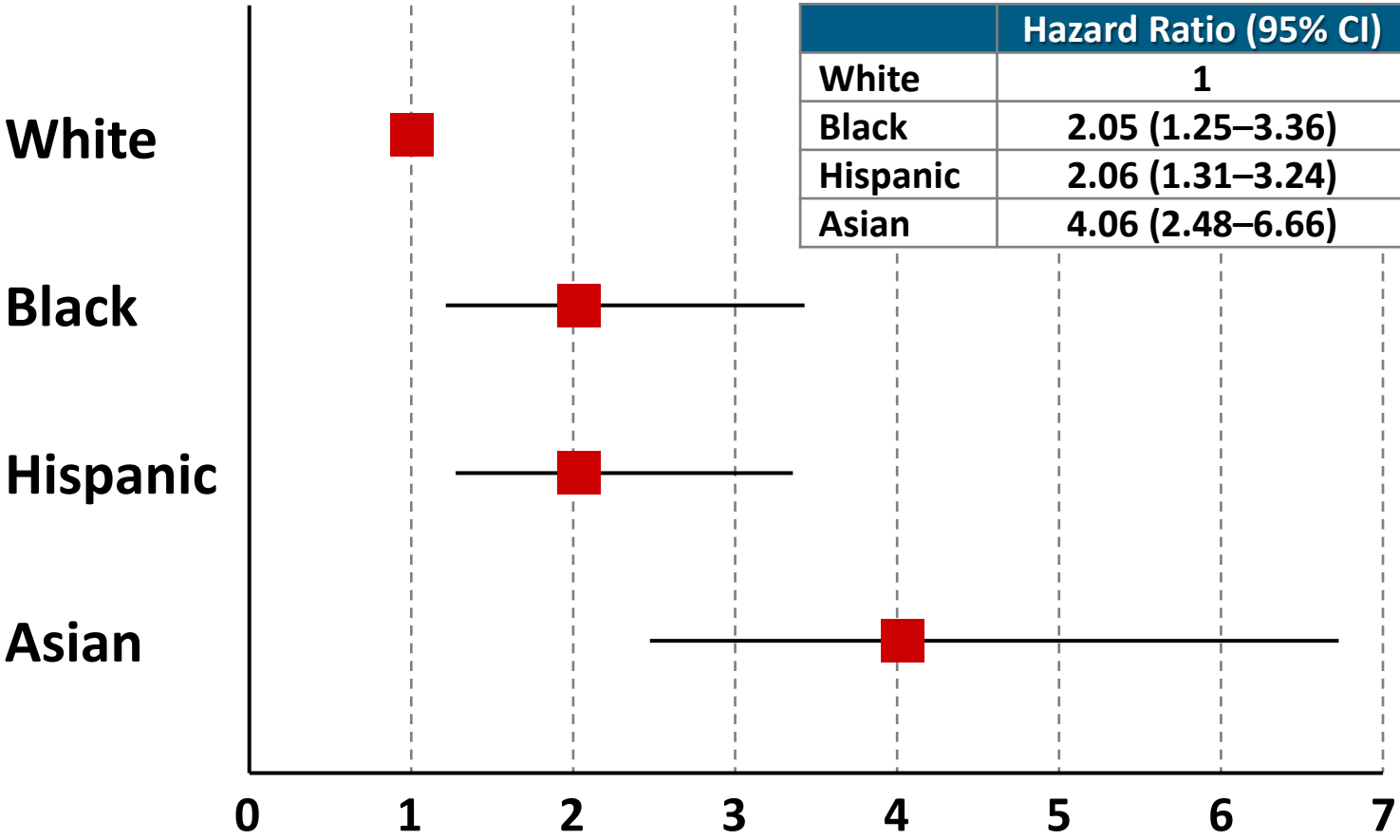


Adjusted Hazard Ratio for ICH on warfarin

Multiethnic cohort of 18,867 patients hospitalized with first-time AF (January 1995 – December 2000)

Shen AY, et al: J Am Coll Cardiol 50: 309-315, 2007

	Hazard Ratio (95% CI)	p Value
White	1	-
Black	2.05 (1.25–3.36)	0.005
Hispanic	2.06 (1.31–3.24)	0.002
Asian	4.06 (2.48–6.66)	<0.0001



Background

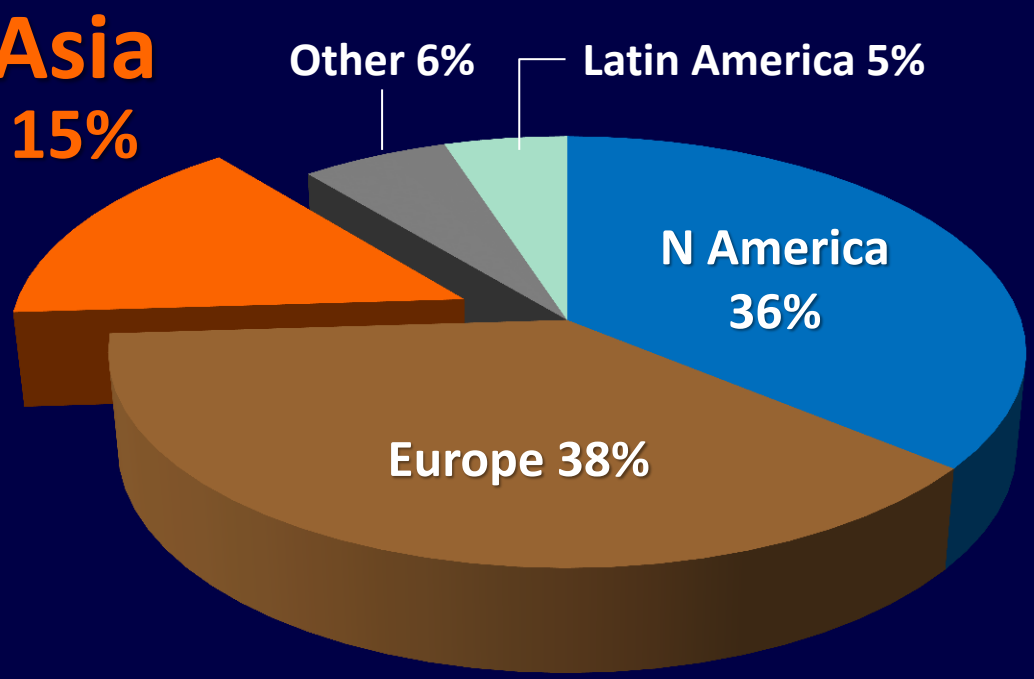
- Incidence of ischemic stroke and bleeding including ICH may not be identical among different ethnic groups.
- The rate of ICH is reported to be higher in Asians than in whites[1,2].
- In RE-LY (randomized control trial, consisting of 18,113 patients) 2,782 patients are from Asian countries[3,4].
- Since RE-LY includes a large number of Asian patients, this control trial is suitable for analyzing the ethnic difference between Asian and non-Asian countries.

1. Shen AY, et al.: J Am Coll Cardiol 50, 309-315, 2007
2. van Asch CJ, et al.: Lancet Neurol 9, 167-176, 2010
3. Connolly SJ, et al.: N Engl J Med 361, 1139-1151, 2009
4. Connolly SJ, et al.: N Engl J Med 363, 1875-1876, 2010

RE-LY® - Recruitment by Region, N=18,113

RE-LY® Asian Countries

	Patients (n)
Total	**2,782**
East Asia	**1,648**
China	541
Hong Kong	90
Japan	326
South Korea	**336**
Taiwan	355
South Asia	**1,134**
India	578
Malaysia	185
Philippines	157
Singapore	59
Thailand	155



Patients Characteristics -1

	Asia (n=2,782)	Non-Asia (n=15,331)
Age (yr)*	68.0±9.8	72.1±8.3
<65 (%)	26.8	14.6
65-74 (%)	45.8	43.2
≥75 (%)	27.4	42.2
Weight (Kg)*	66.3±12.8	85.6±19.2
Blood pressure (mmHg)		
Systolic*	129±17.5	131±17.4
Diastolic*	78±10.7	77±10.5
Male sex (%)	63.8	63.5
Type of atrial fibrillation		
Paroxysmal(%)	27.7	33.7
Persistent (%)	41.4	30.3
Permanent (%)	30.9	36.0
Creatinine clearance (mL/min)*	65.3±22.1	74.2±28.1
<50 (%)	26.6	18.3
50-79 (%)	51.3	46.5
≥80 (%)	21.8	34.2

*: mean±SD

Patients Characteristics -2

	Asia (n=2,782)	Non-Asia (n=15,331)
$CHADS_2$ score (mean±SD)	2.2±1.1	2.1±1.1
0-1 (%)	30.2	32.3
2 (%)	33.0	36.1
3-6 (%)	36.8	31.6
Previous stroke (%)	24.2	10.4
Prior myocardial infarction (%)	9.3	17.9
Heart failure (%)	36.3	31.2
Diabetes mellitus (%)	25.1	23.0
Hypertension (%)	71.2	80.2
Medicine in use at baseline		
Aspirin (%)	47.1	38.1
ARB (%)	32.9	22.3
ACE-I (%)	28.4	47.8
Beta-blocker (%)	46.2	66.0
Amiodarone (%)	14.2	10.3
Verapamil (%)	4.7	6.1
Proton pump inhibitor (%)	8.0	15.3
H_2 blocker (%)	5.6	3.9
Long-term VKA therapy experience (%)	36.5	52.0

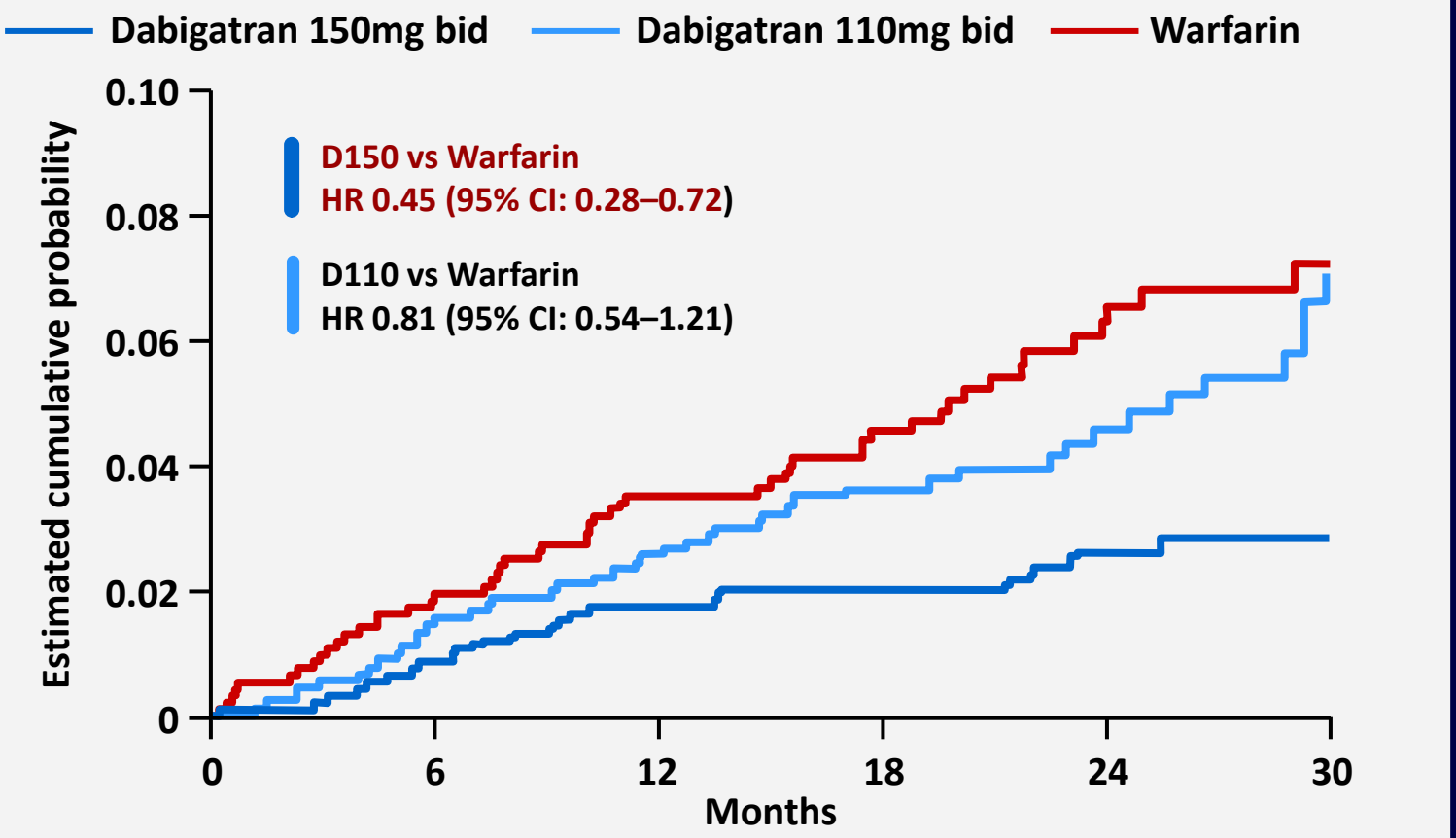
INR Control

	Asia (n=880)			Non-Asia (n=4,909)		
INR	**< 2**	**2-3**	**> 3**	**< 2**	**2-3**	**> 3**
Mean	35.4	54.5	10.1	19.8	66.2	14.0
Median	30.8	56.5	8.1	15.4	68.9	11.6

INR 2-3

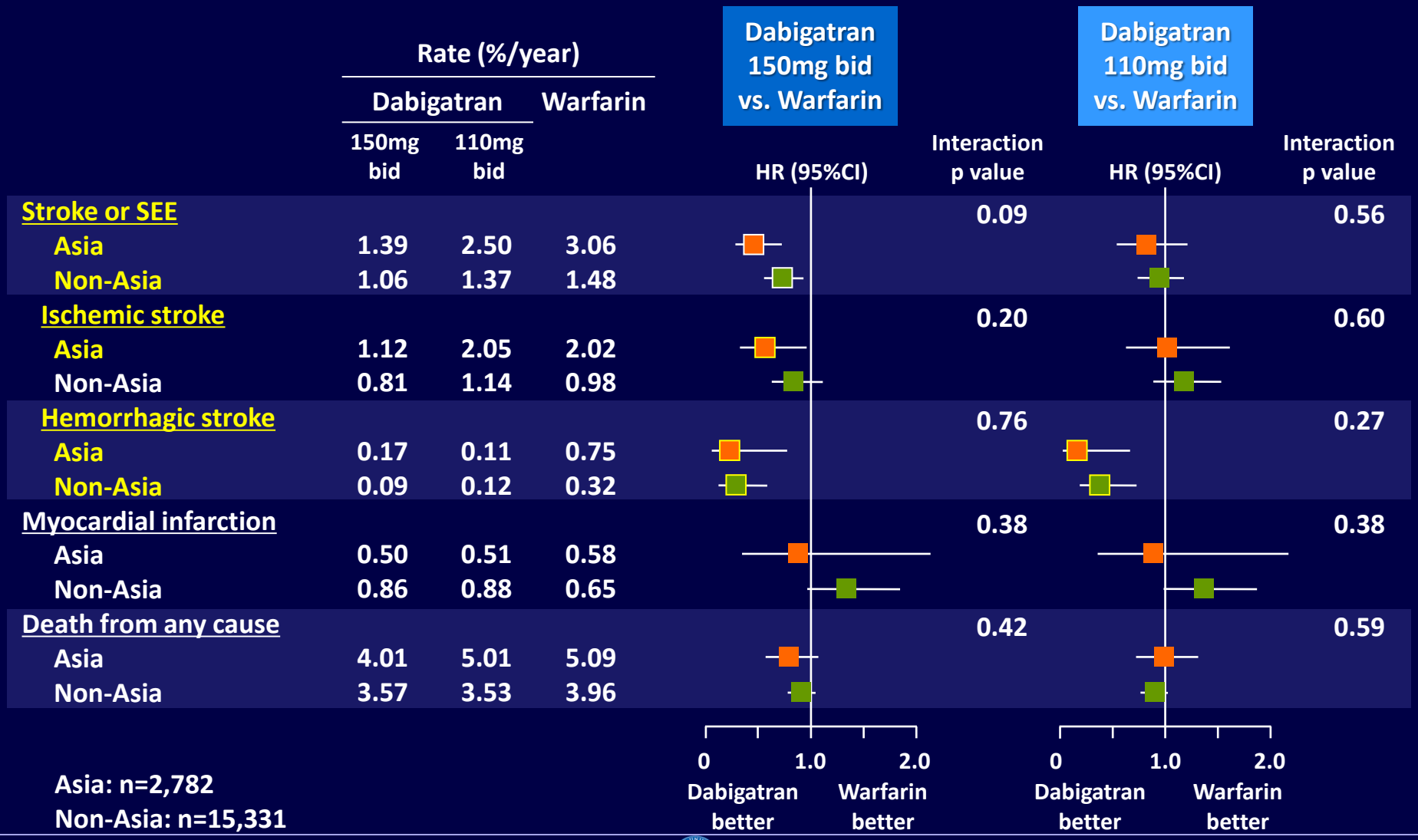
Asia	Mean: 54.5, Median: 56.5
Non-Asia	Mean: 66.2, Median: 68.9

Cumulative Hazard Rates for Stroke or Systemic Embolism in Asian



Subjects at risk						
DE 150mg bid	933	906	875	697	420	237
DE 110mg bid	923	888	866	683	401	216
Warfarin	926	886	858	664	382	198

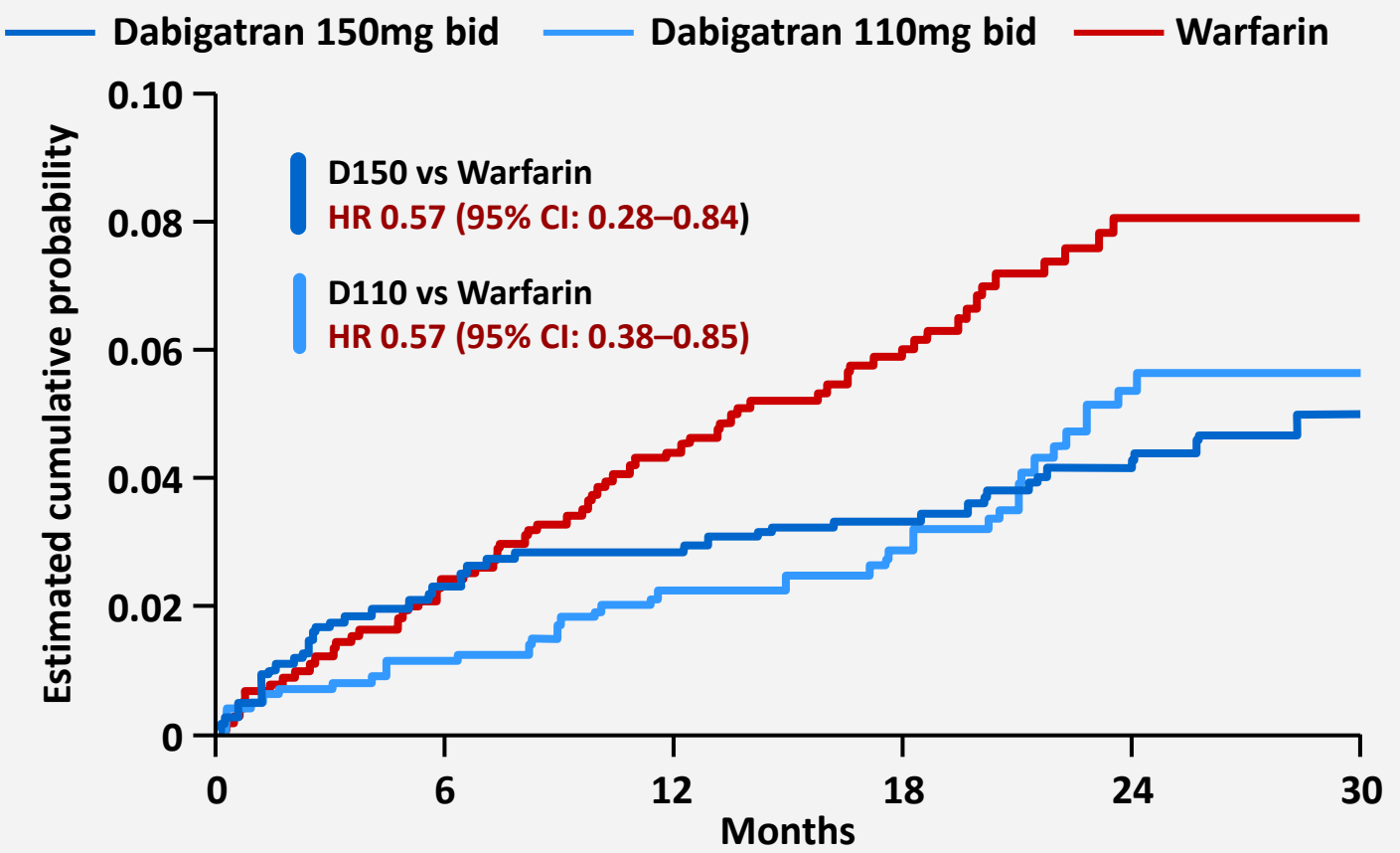
Interaction to Efficacy (Asian vs Non-Asian)



Asia: n=2,782

Non-Asia: n=15,331

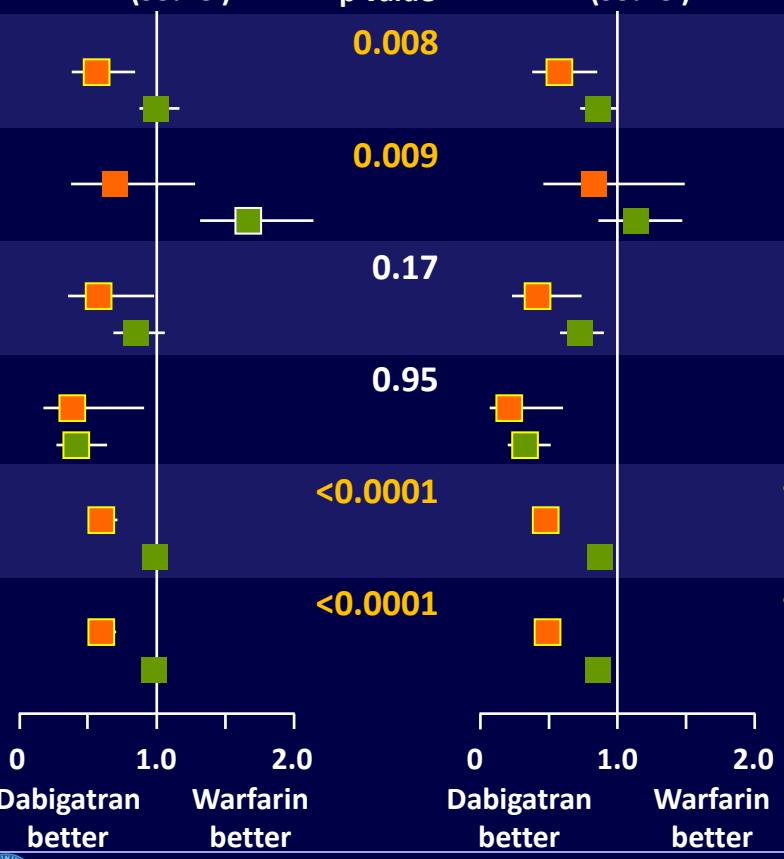
Cumulative Hazard Rates for Major Bleeding in Asia



Subjects at risk						
DE 150mg bid	933	896	869	693	419	237
DE 110mg bid	923	889	863	685	400	219
Warfarin	926	884	850	658	374	191

Interaction to Safety (Asian vs Non-Asian)

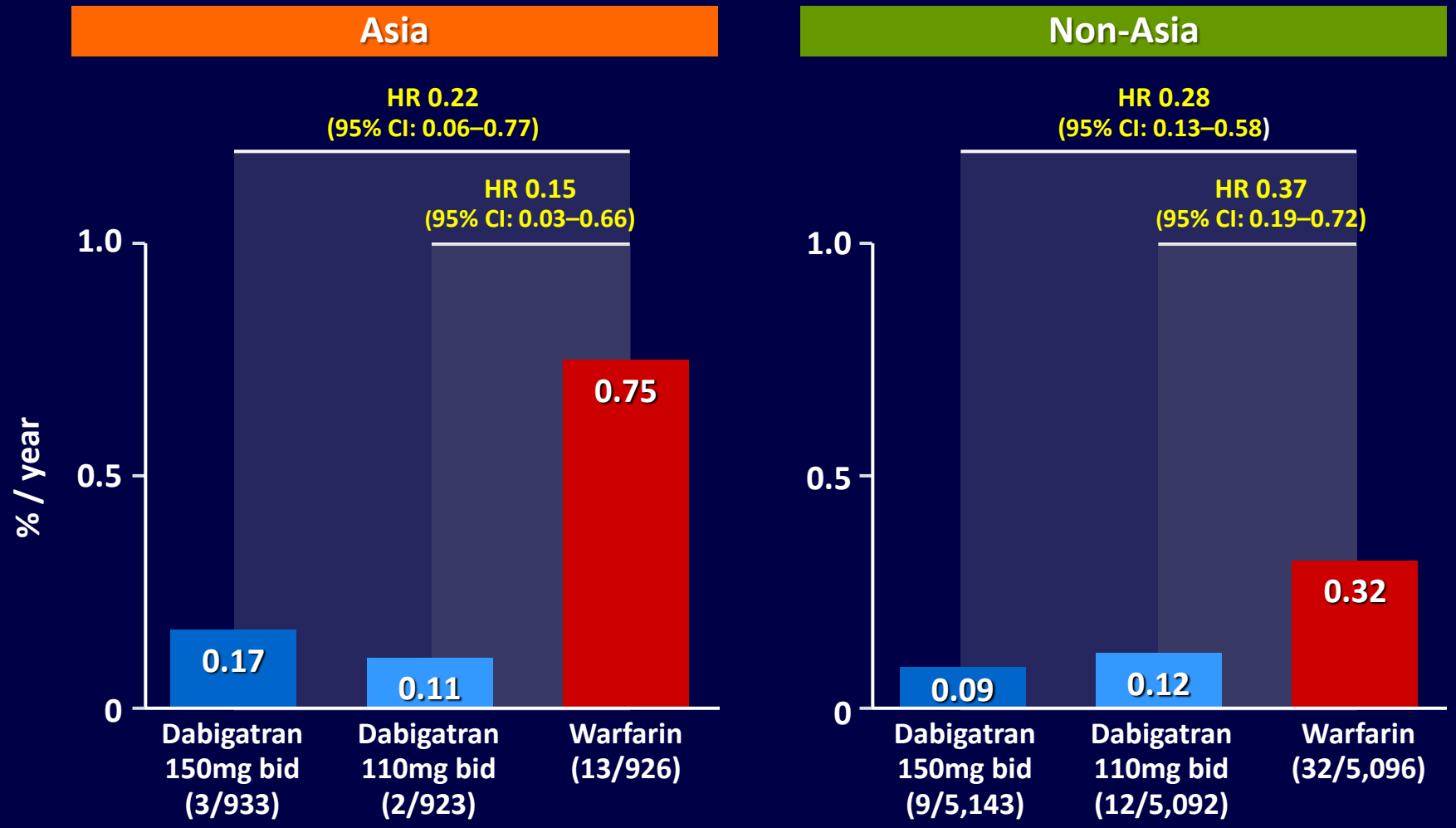
	Rate (%/year)			Dabigatran 150mg bid vs. Warfarin		Dabigatran 110mg bid vs. Warfarin	
	Dabigatran		Warfarin				
	150mg bid	110mg bid		HR (95%CI)	Interaction p value	HR (95%CI)	Interaction p value
Major bleeding					0.008		0.07
Asia	2.17	2.22	3.82				
Non-Asia	3.52	2.99	3.53				
GI major bleeding					0.009		0.34
Asia	0.96	1.15	1.41				
Non-Asia	1.69	1.14	1.01				
Life threatening bleeding					0.17		0.07
Asia	1.28	0.91	2.20				
Non-Asia	1.52	1.29	1.79				
Intracranial bleeding					0.95		0.46
Asia	0.45	0.23	1.10				
Non-Asia	0.29	0.23	0.71				
Minor bleeding					<0.0001		<0.0001
Asia	12.43	10.12	19.66				
Non-Asia	15.27	13.69	15.81				
Major or minor bleeding					<0.0001		<0.0001
Asia	13.99	11.72	22.03				
Non-Asia	17.02	15.27	17.74				



Asia: n=2,782

Non-Asia: n=15,331

Hemorrhagic Stroke



Summary

- The effects of dabigatran against stroke or systemic embolism are comparable in Asian and non-Asian patients for both doses of dabigatran compared to warfarin.

- Reduction in major bleeding with dabigatran, compared with warfarin, was greater in Asian patients.

- Although Asian patients had considerably more time below therapeutic range and were younger than non-Asian patients, there was a trend for more bleeding in Asians on warfarin.

Discrepancy Between $CHADS_2$ score and CHA_2DS_2-VASc score in Anticoagulation for AF

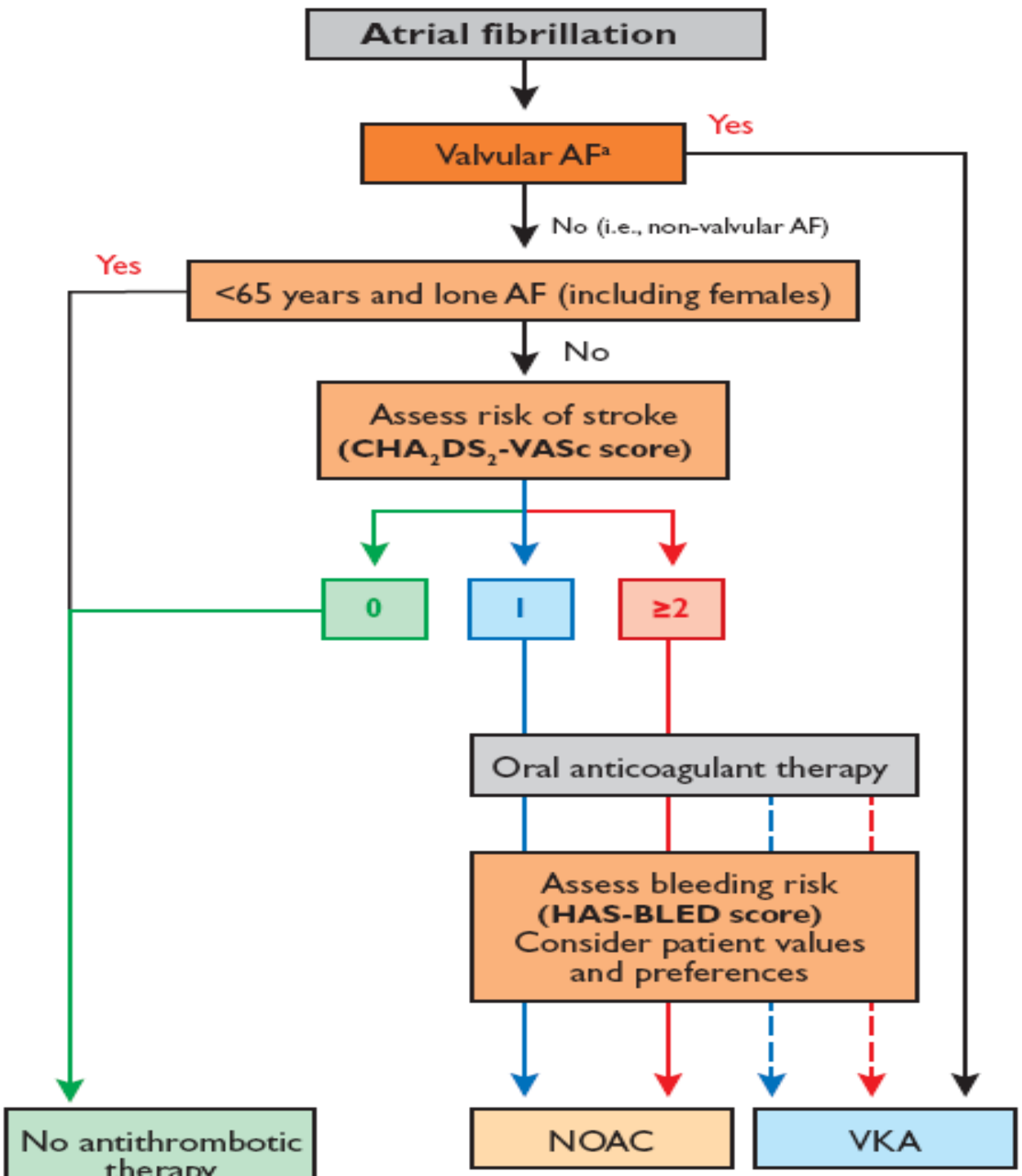
2012 ES

In patients with a CHA_2DS_2-VASc score ≥2, C
- adjusted-dose VKA (INR 2–3); or
- a direct thrombin inhibitor (dabigatran);
- an oral factor Xa inhibitor (e.g. rivaroxa

… is recommended, unless contraindica

When adjusted-dose VKA (INR 2–3) cannot difficulties in keeping within therapeutic antic undertake INR monitoring, one of the NOAC
- a direct thrombin inhibitor (dabigatran);
- an oral factor Xa inhibitor (e.g. rivaroxa

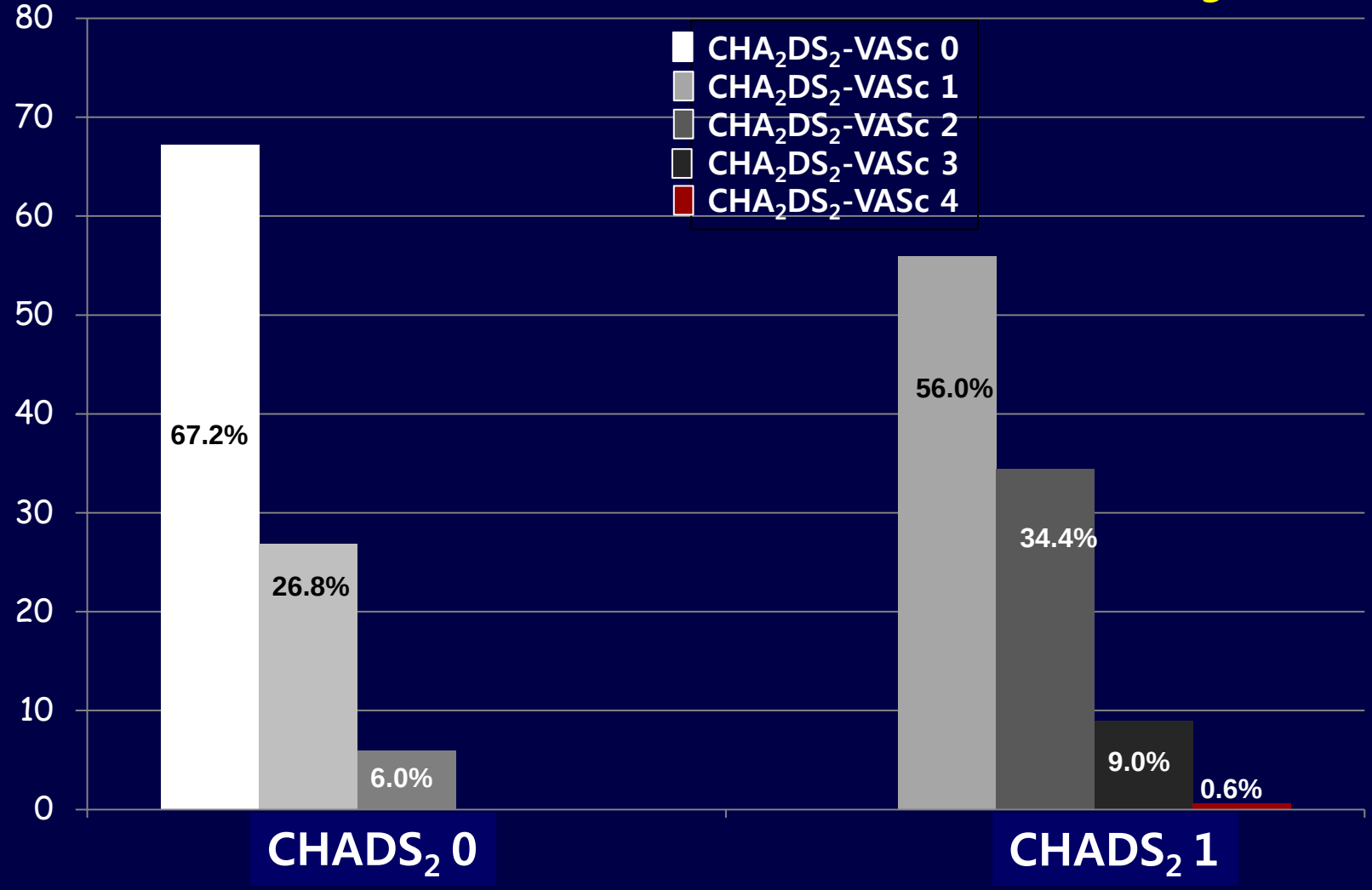
… is recommended.



Difference in $CHADS_2$ vs. CHA_2DS_2-VASc

(n=1004; Yonsei AF Ablation Cohort)

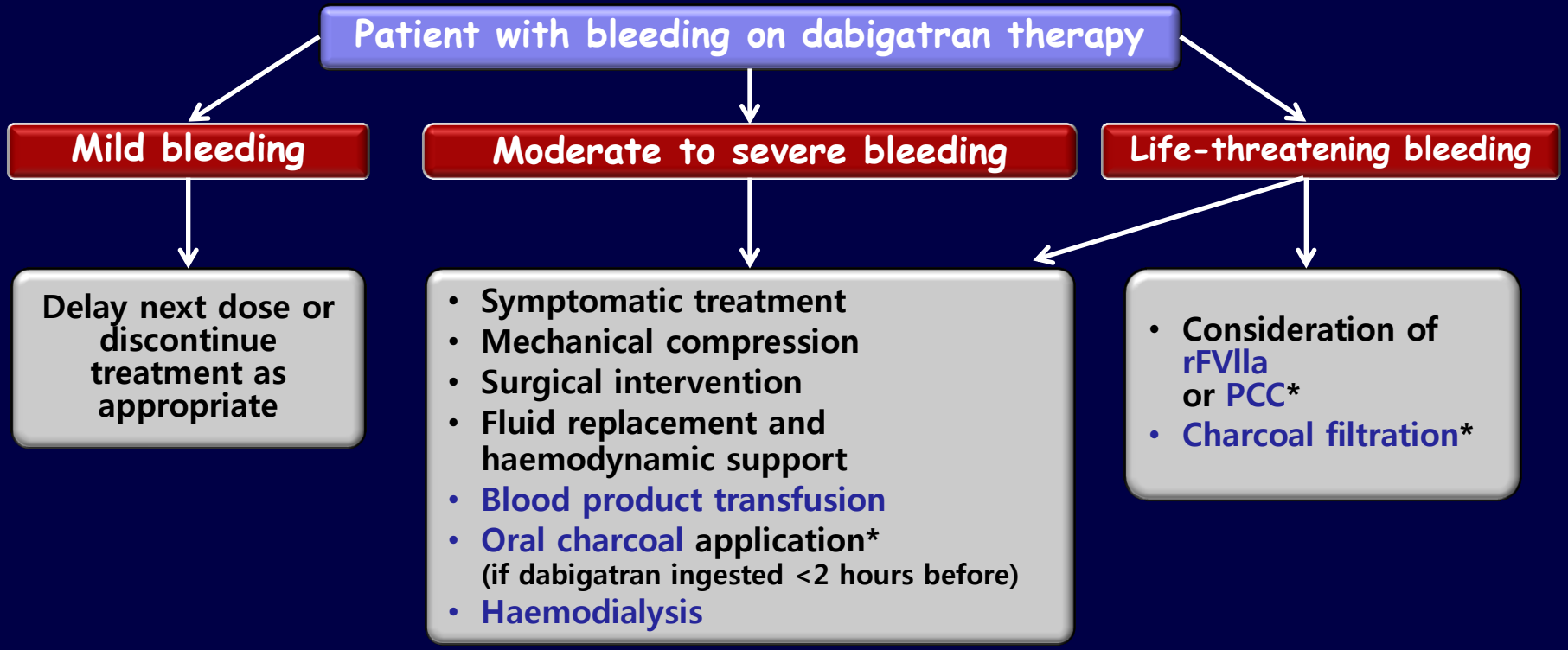
CHADS2 score 기준 ASA 사용하던 환자의 32.8%~61.9%가 anticoagulation Ix



Management & Outcomes of Major Hemorrhage on Dabigatran vs. Warfarin

Reversing the effects of dabigatran by coagulation factor concentrates (CFCs)

- There is some experimental evidence to support the role of CFCs in reversing the anticoagulant effect of dabigatran (e.g. in cases of overdose or major bleeding)*



*PCC = prothrombin complex concentrate; rFVIIa = recombinant activated Factor VIIa;

Patient population: Phase III dabigatran trials – methods

Phase III trial	Patients	Treatments	Duration of treatment
RE-LY®[1]	18 113 patients with AF (stroke prevention)	• Dabigatran 110 mg • Dabigatran 150 mg BID • Warfarin	Median 2 years
RE-COVER™[2]	2539 patients with VTE (treatment)	• Dabigatran 150 mg BID • Warfarin	6 months
RE-COVER II™[3]	2568 patients with VTE (treatment)	• Dabigatran 150 mg BID • Warfarin	6 months
RE-MEDY™[4]	2856 patients with VTE (secondary prevention)	• Dabigatran 150 mg BID • Warfarin	Mean, 15.5 months
RE-SONATE™[5]	1343 patients with VTE (secondary prevention)	• Dabigatran 150 mg BID • Placebo	6 months
Patients randomized and treated in these five trials: N=27 419 (**dabigatran n=16 755; warfarin n=10 002; placebo n=662**)			

Key criteria for inclusion in bleeding case narrative analysis:
only centrally adjudicated major bleeding within 3 days of the last dose

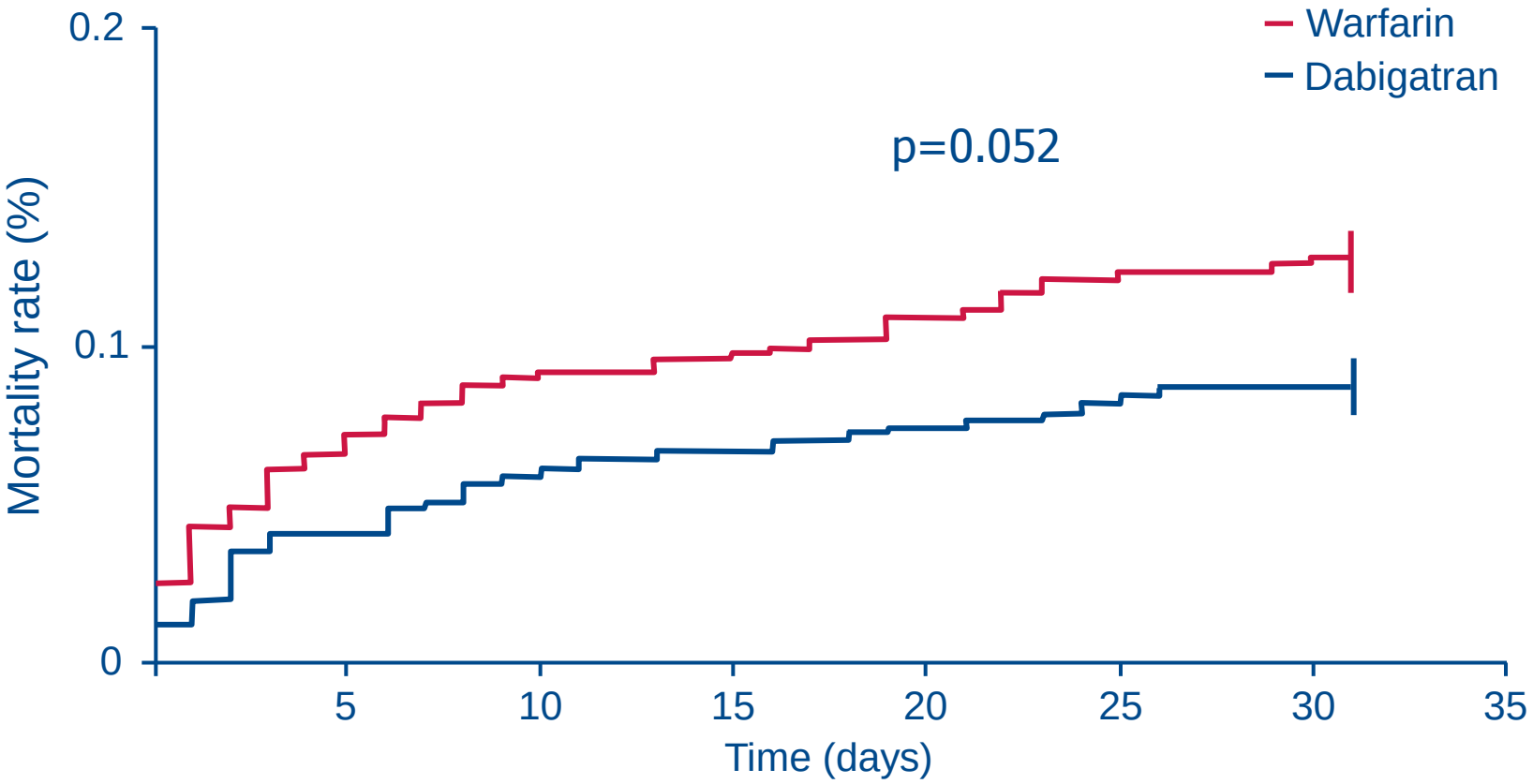
Patient characteristics: five Phase III trials – results

Patient characteristics	Dabigatran*	Warfarin	P value
Patients with major bleeding, n	627	407	
Age, years, mean (SD)	75.3 (7.3)	71.8 (10.3)	<0.0001
Male sex, n (%)	404 (64.4)	268 (65.9)	0.66
Body weight, kg, mean (SD)	81.8 (19.6)	81.2 (20.5)	0.63
CrCl, mL/min, median (range)	53 (5–199)	62 (7–239)	<0.0001
ASA, n (%)	194 (30.9)	100 (24.6)	0.026
Clopidogrel, n (%)	12 (1.9)	7 (1.7)	1.0
Triple therapy, n (%)	23 (3.7)	14 (3.4)	0.93
NSAID, n (%)	81 (12.9)	34 (8.4)	0.023

Strategies used for management of major bleeding: RE-LY® trial – results

	Dabigatran*	Warfarin	P value
Patients with major bleeds, n (%)	741 (100)	421 (100)	
Blood transfusion, n (%)	439 (59.2)	210 (49.9)	0.002
Fresh frozen plasma, n (%)	147 (19.8)	127 (30.2)	<0.001
Vitamin K, n (%)	70 (9.4)	115 (27.3)	<0.001
Prothrombin complex concentrate, n (%)	5 (0.7)	5 (1.2)	0.36
Recombinant Factor VIIa, n (%)	8 (1.1)	3 (0.7)	0.53

Mortality after a major bleed: five Phase III trials – results

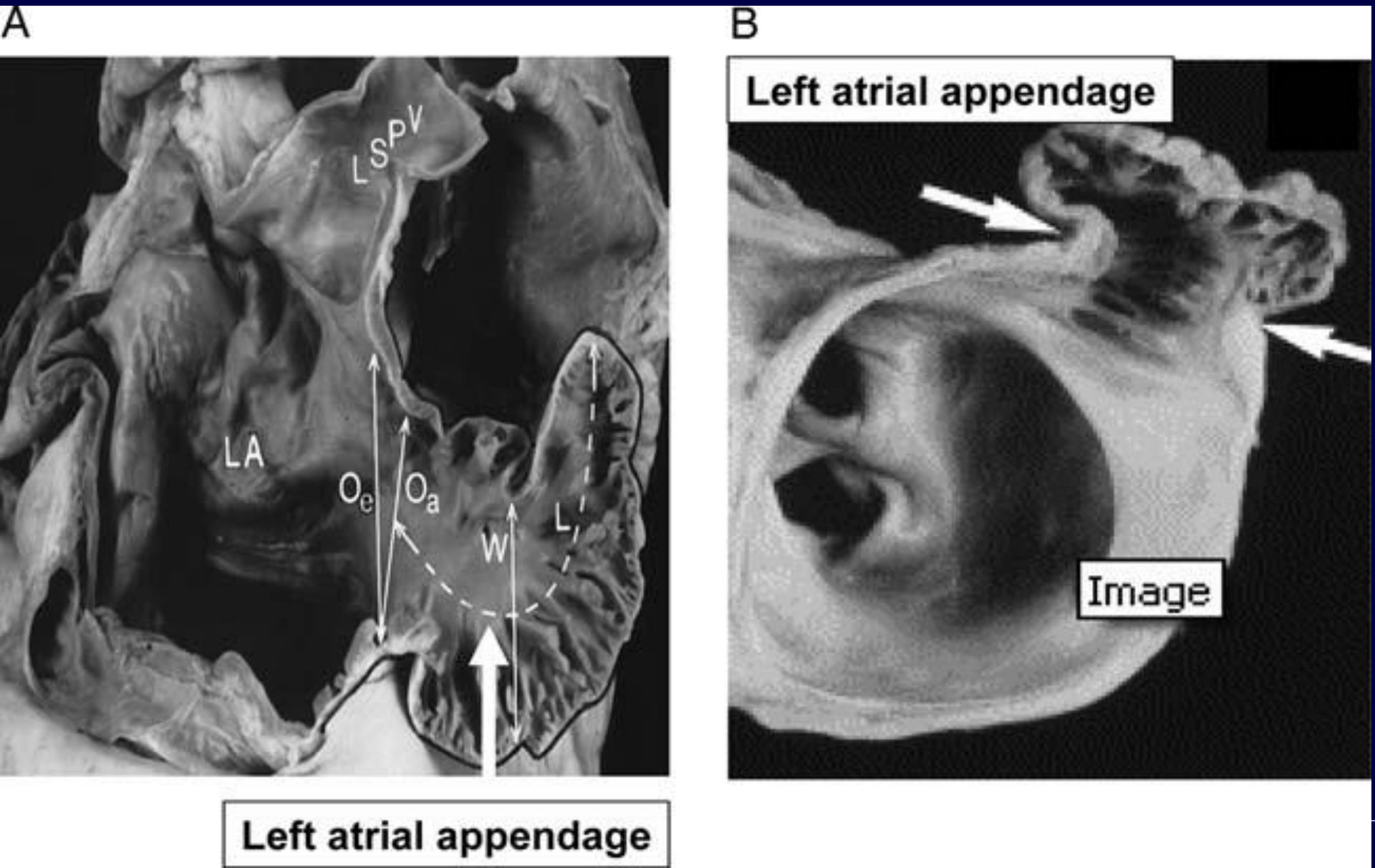


Summary

- Despite the unavailability of a specific antidote against dabigatran, the overall resources required to manage bleeding are not greater.
- The management of severe bleeding on dabigatran can be further improved by access to a specific antidote, which is in development.

How to Manage the Patients with High Risk of Stroke, but Hemorrhagic Complications?

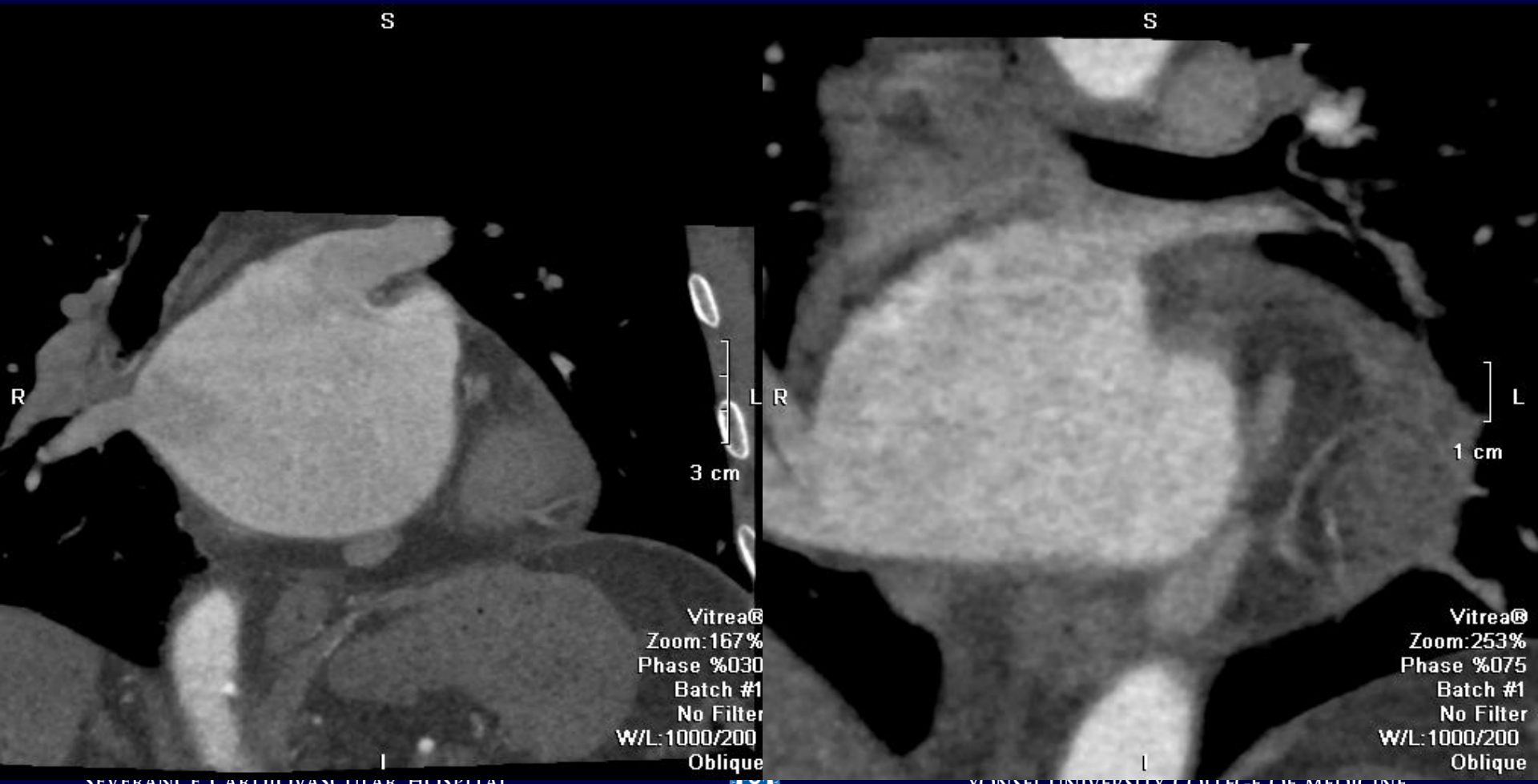
Blackshear JL, et al. Ann Thorac Surg 1996;61:755–759.
Landmesser U, et al. Eur Heart J 2012;33:698-704.



Pre- & Post-Procedural CT

Follow-up Schedule:
Warfarin 45days – TEE (<5mm) – ASA+Clopidogrel 6Mo – ASA 81~325mg only

WATCHMAN **ACP**



Usefulness of 3D TEE

Kim YL, Pak HN, et al. YMJ 2012;53(1):83-90.

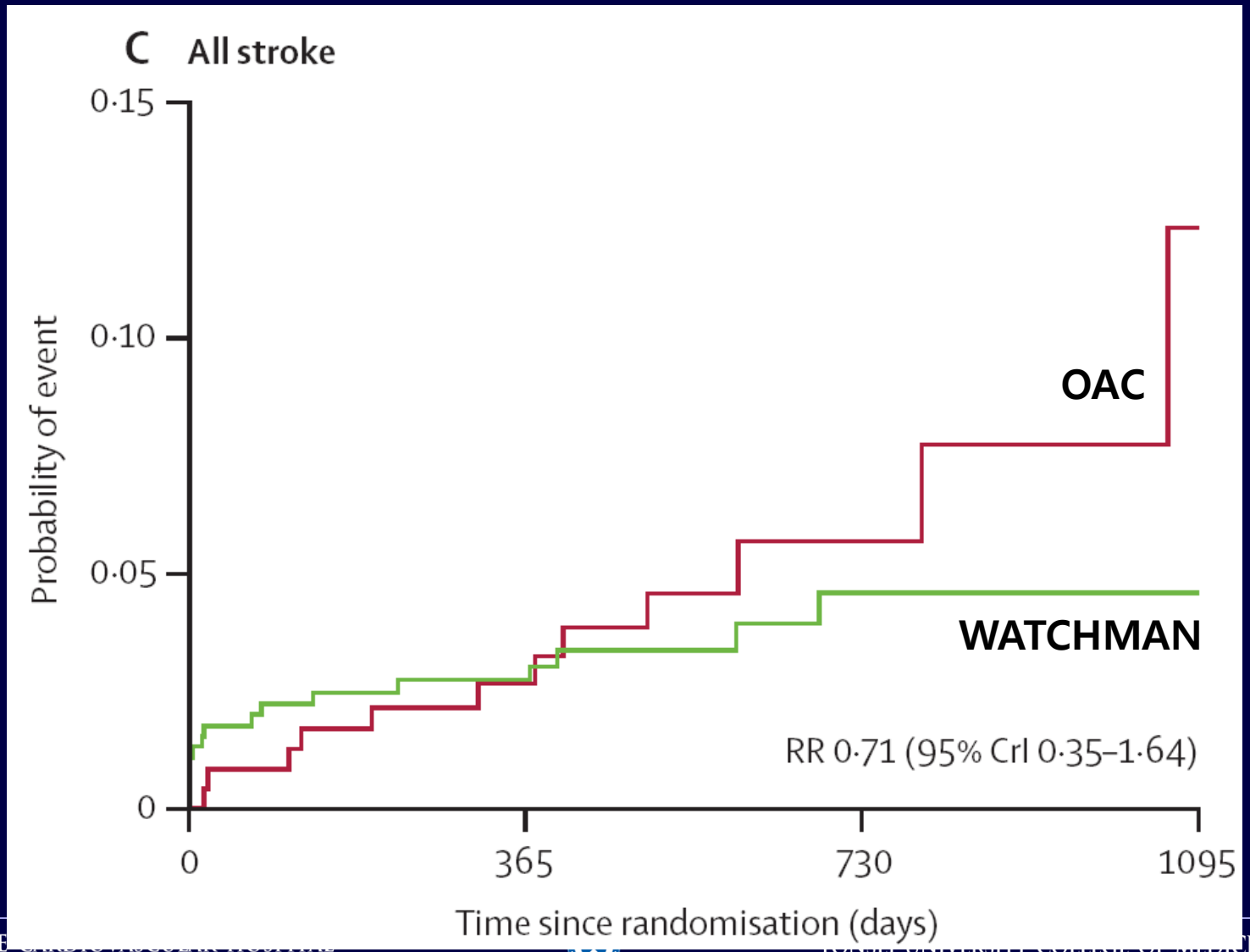
WATCHMAN

ACP

Pak HN et al. Can J Cardiol. 2012;[In Press]

Risk of Stroke After LAA-OD

PROTECT AF Investigators. Lancet 2009; 374: 534–42



Clinical Trials for LAA-OD

	PROTECT AF[1,2]	CAP[2]	ASAP[3,4]	PREVAIL
Control	Patients able to take warfarin		Warfarin contraindicated patients	Patients able to take warfarin
Primary Endpoint	All stroke, systemic embolism and cardiovascular death	All stroke, systemic embolism and cardiovascular death	All stroke, systemic embolism, and cardiovascular death	All stroke, systemic embolism and cardiovascular death
Mean age /CHADS	72/2.2	74/2.4	72.4/2.8	ongoing
Total Enrolled Subjects	707 randomized[1], 93 pts rolled in[2]	460	150	400
Total Patients Implanted	542[2]	437	142	
Implantation Success	89.5%[2]	95.0%	94.7%	
Warfarin discontinuation at 45 days	86.6%	94.9%	No warfarin used	
Stroke	Rate ratio 0.71 (0.35–1.64) [Hemorrhagic Stroke: 0.09 (0.00–0.45)]	Reduction in procedure related stroke vs PROTECT AF (*P*=0.04)	Decreased rate of stroke by 77% vs. expected rate per $CHADS_2$ Score	
Bleeding	HR 1.69 (1.01–3.19)	Reduction in pericardial effusions vs PROTECT AF (*P*=0.02)	Pericardial effusion with tamponade=2.0% Major bleeding=2.7%	

1. Holmes DR et al. *Lancet* 2009;374:534–42, 2. Reddy VY et al. *Circulation*. 2011;123:417-424 3. Sievert H. TCT 2011, 4. Reddy, HRS 2012,

Yonsei Experiences for LAA-OD

- 23 patients with permanent AF
  - 74% males, 65.1±10.1 years
  - 10 Failed Rhythm control
  - 16 past history of stroke or embolism
  - LA size 52.3±8.5mm, EF 61.4±10.4%

- Risk of Stroke & Bleeding
  - $CHADS_2$ score 3.1±0.8
  - HAS-BLED score 3.7±1.5
  - $CHADS_2$ + HAS-BLED 6.8±2.1

Yonsei Experiences for LAA-OD

- Acute Procedural Success Rate
  - No procedure failure
  - 1 case of respiratory arrest & successful CPR
  - No acute complication, no pericardial effusion

- 17.2±9.3 months FU
  - No device failure or leak at 8 week TEE
  - Stop OAC in 17/23 patients after FU TEE
  - One patient with severe SEC is continuing OAC.
  - Five patients within 45 days after procedure.

Take-Home Message

- Dabigatran is the best option for anticoagulation in patients with AF and CHA2DS2-VASc score ≥ 1, even in over 4 years follow-up data (RELY-ABLE).
- Dabigatran is better for the prevention of ischemic stroke with lower risk of hemorrhagic complication than warfarin, especially in Asian.
- In AF patients with high CHA2DS2-VASc score and high HAS-BLED score, left atrial appendage occlusion device should be considered.