Subgroup Analysis from the RE-DUAL PCI Trial

Dual Antithrombotic Therapy with Dabigatran in Patients with Atrial Fibrillation Undergoing Percutaneous Coronary Intervention

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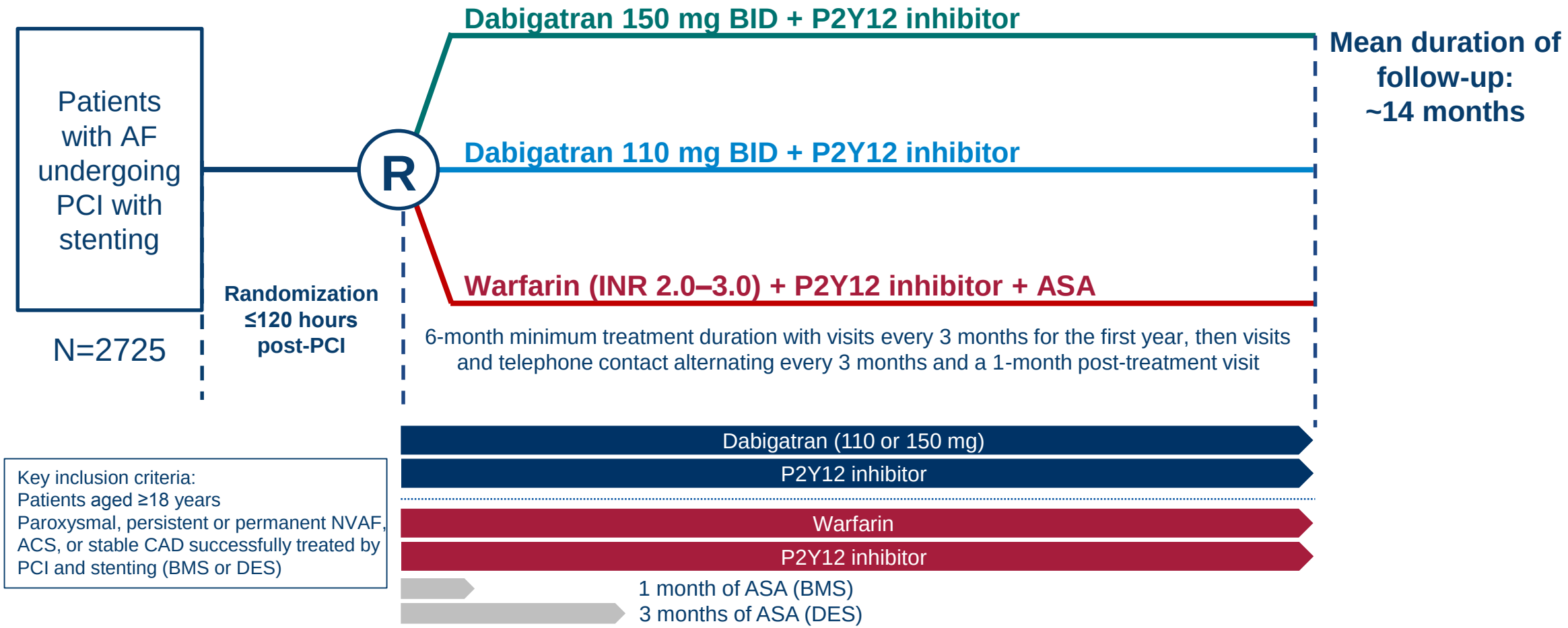
on behalf of the RE-DUAL PCI Steering Committee and Investigators

Disclosures

Dr Oldgren reports consultant and lecture fees to his institution from Boehringer Ingelheim, Bayer, Bristol-Myers Squibb, Daiichi-Sankyo, Pfizer, and Sanofi.

Study design: multicenter, randomized, open-label trial following a PROBE design

RE-DUAL PCI
Study in NVAF patients undergoing PCI



Key inclusion criteria:
Patients aged ≥18 years
Paroxysmal, persistent or permanent NVAF, ACS, or stable CAD successfully treated by PCI and stenting (BMS or DES)

Patients aged <80 yr (<70 yr in Japan) were randomized to dabigatran 110 or 150 dual therapy, or warfarin triple therapy.
Patients aged ≥80 yr in the United States were randomized to dabigatran 110 or 150 dual therapy, or warfarin triple therapy in a 1:1:1 ratio.
Patients aged ≥80 yr in other countries (≥70 yr in Japan) were randomized to dabigatran 110 dual therapy or warfarin triple therapy in a 1:1 ratio.

ACS, acute coronary syndrome; AF, atrial fibrillation; ASA, acetylsalicylic acid; BID, twice daily; BMS, bare-metal stent; CAD, coronary artery disease; DES, drug-eluting stent; INR, international normalized ratio; NVAF, non-valvular atrial fibrillation; PCI, percutaneous coronary intervention; PROBE, prospective, randomized, open, blinded endpoint.

Cannon et al. Clin Cardiol. 2016;39(10):555-564.

Primary Endpoint: time to first ISTH major or clinically relevant non-major (CRNM) bleeding event

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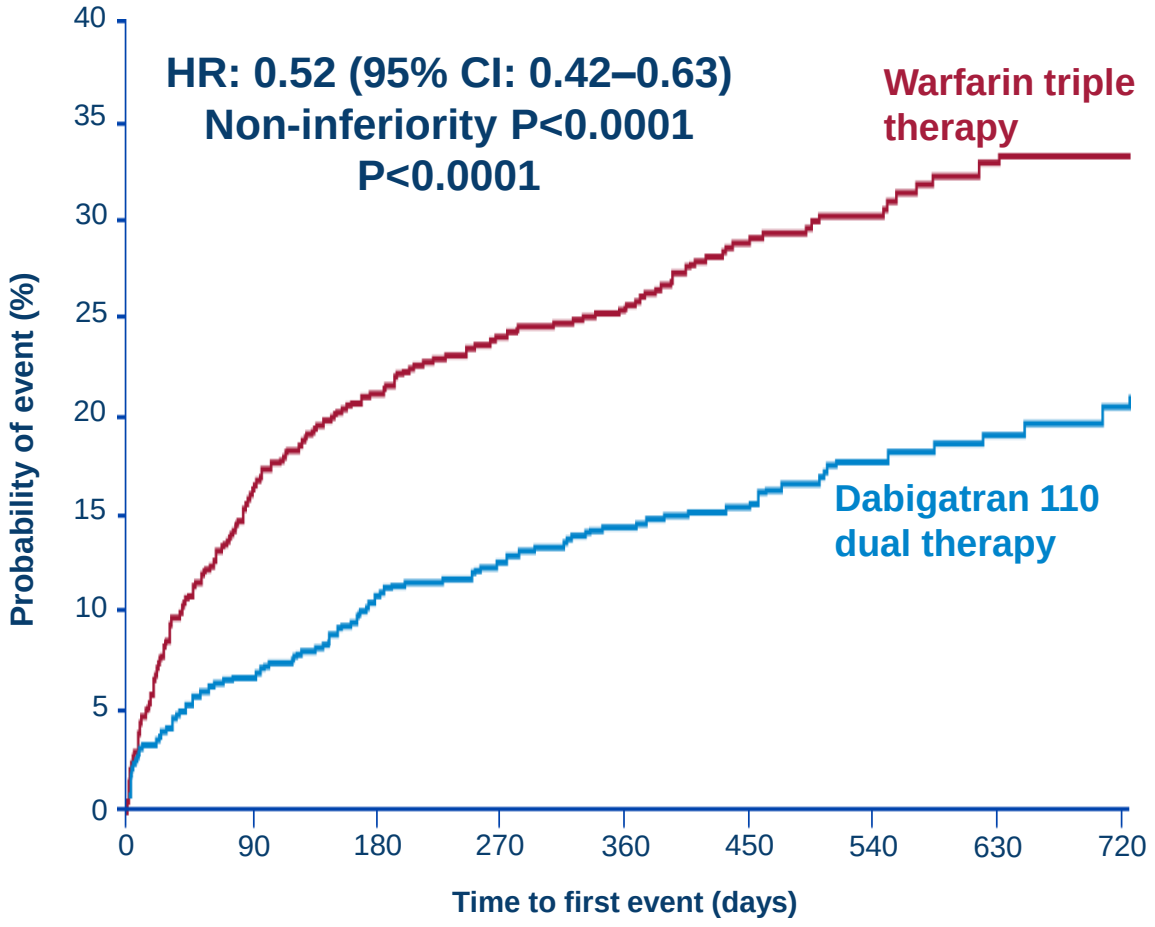
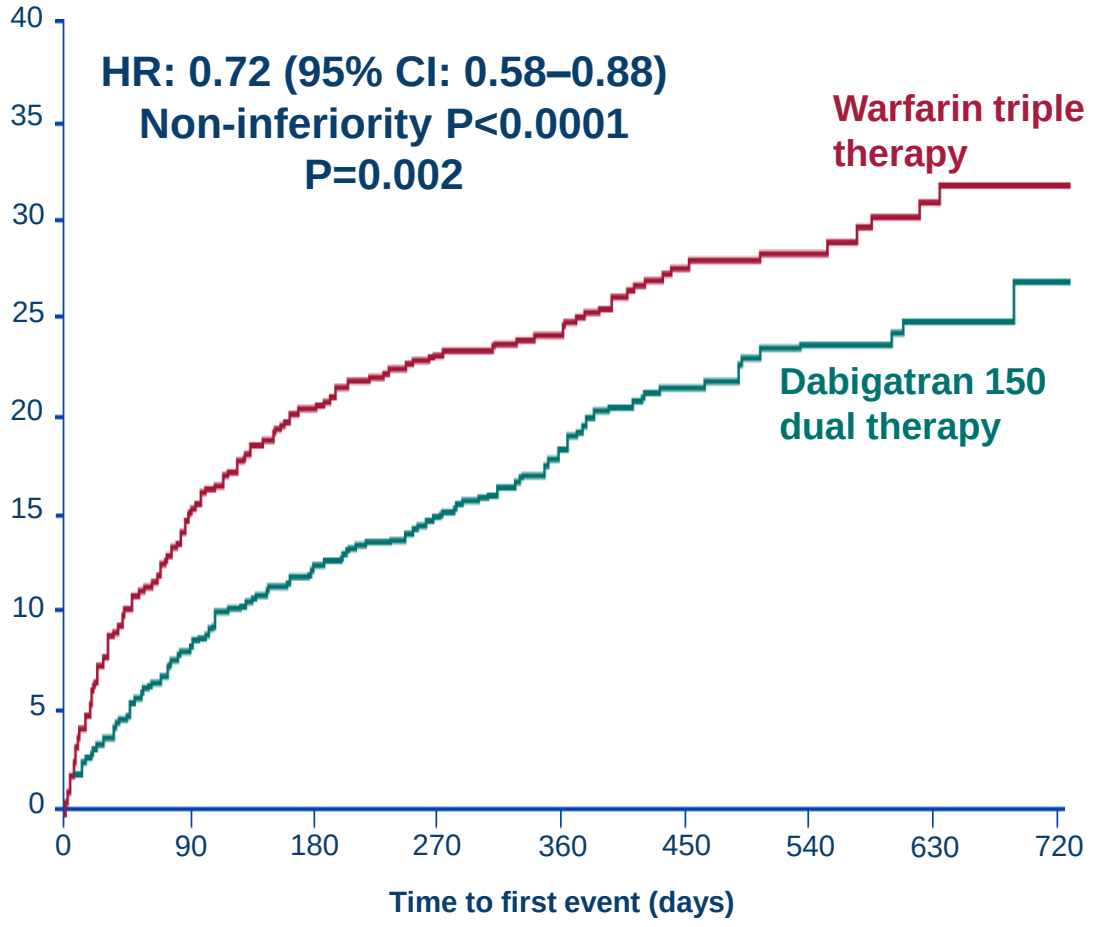
Study in NVAF patients undergoing PCI





Full analysis set presented. HRs and Wald CIs from Cox proportional-hazard model. For the dabigatran 110 dual therapy vs warfarin triple therapy comparison, the model is stratified by age, non-elderly vs elderly (<70 or ≥70 years old in Japan and <80 or ≥80 years old elsewhere). For the dabigatran 150 dual therapy vs warfarin triple therapy comparison, an unstratified model is used; elderly patients outside the United States are excluded. Non-inferiority P value is one sided (alpha=0.025). Wald two-sided P value from (stratified) Cox proportional-hazard model (alpha=0.05).
CI, confidence interval; HR, hazard ratio; ISTH, International Society on Thrombosis and Haemostasis.

Cannon et al. NEJM. 2017;377(16):1513-1524.

Composite efficacy outcome –
all-cause death, myocardial infarction, stroke, systemic embolism, or unplanned revascularization

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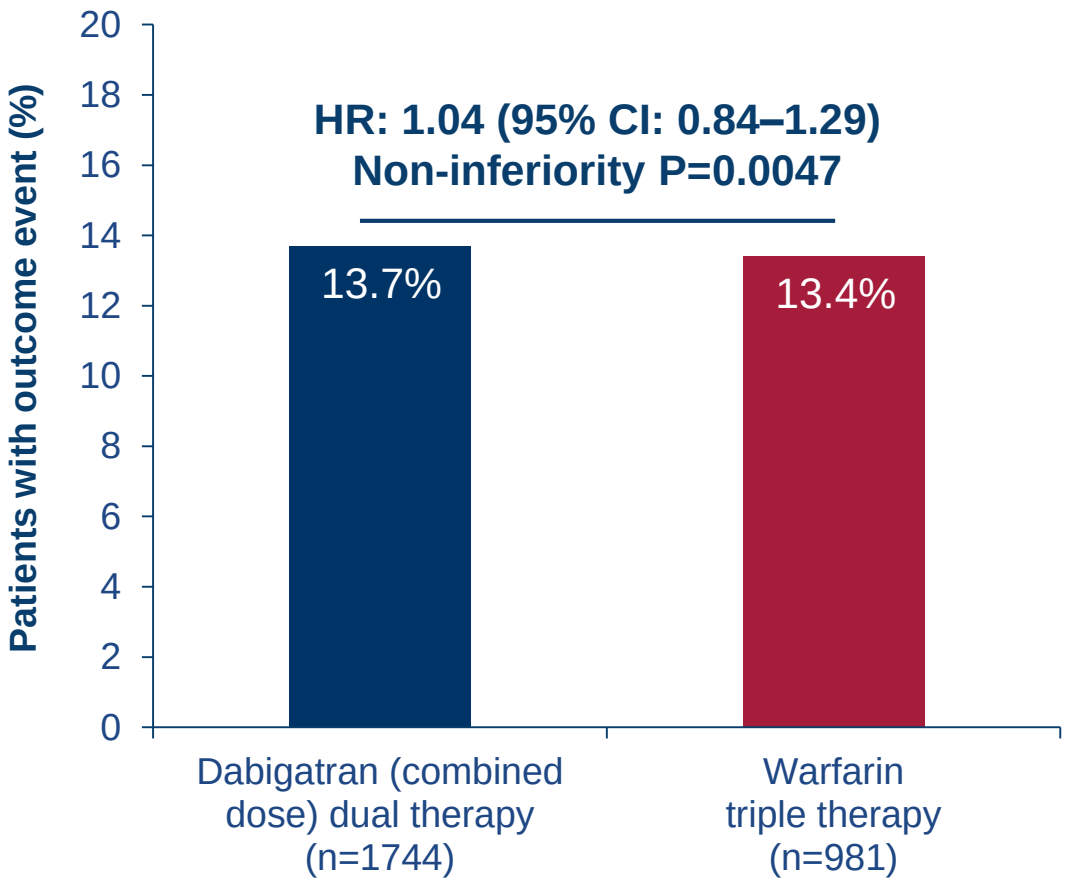

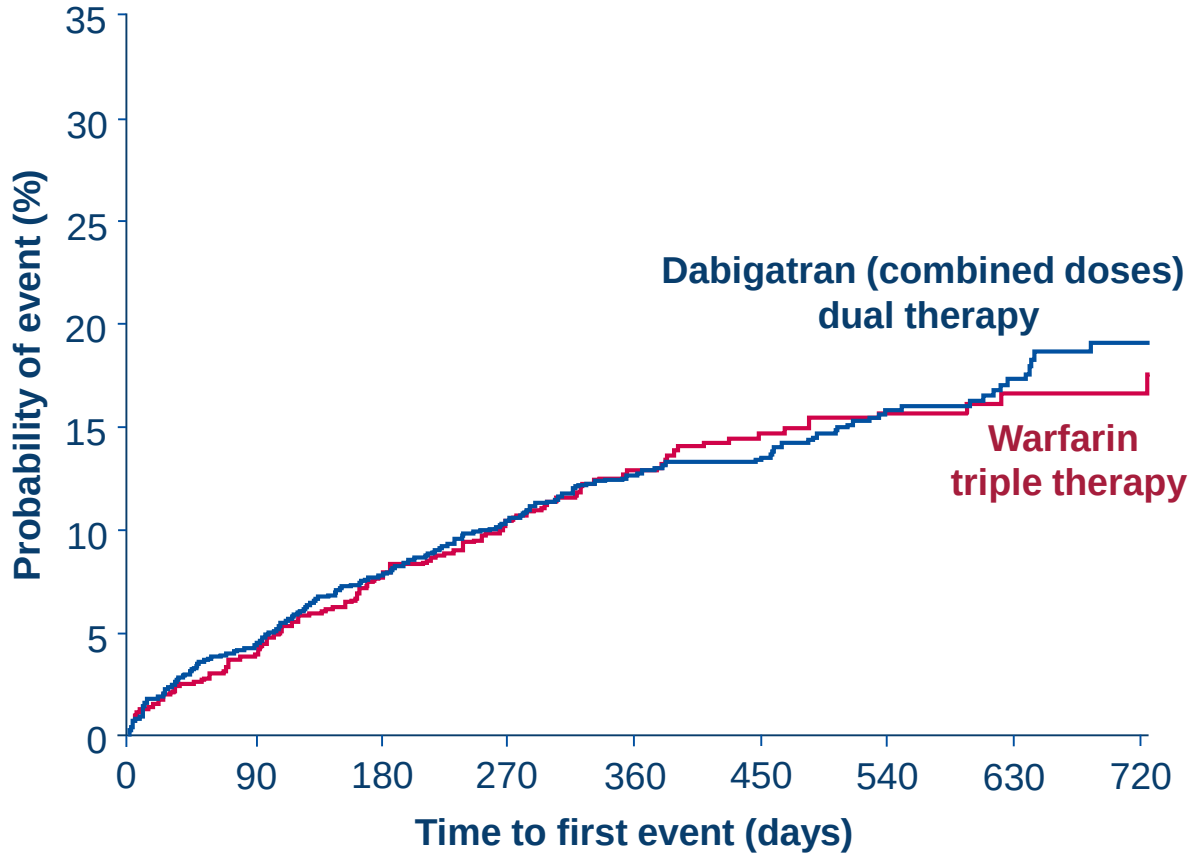

Non-inferiority P value is one sided (alpha=0.025). Results presented are Step 3 of hierarchical testing procedure, testing non-inferiority of dabigatran dual therapy (combined doses) to warfarin triple therapy in death or thromboembolic event and unplanned revascularization. CI, confidence interval; HR, hazard ratio.

Cannon et al. NEJM. 2017;377(16):1513-1524.

ACS vs non-ACS: baseline characteristics

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	ACS (N=1375)	Non-ACS (N=1349)
Mean age, years (SD)	70.9 (9.1)	70.6 (8.1)
Male, n (%)	1010 (73.5)	1059 (78.5)
Atrial fibrillation at baseline, n (%)		
Paroxysmal	708 (51.5)	643 (47.7)
Persistent	229 (16.7)	255 (18.9)
Permanent	437 (31.8)	451 (33.4)
Diabetes, n (%)	492 (35.8)	501 (37.1)
Prior stroke, n (%)	106 (7.7)	120 (8.9)
Prior myocardial infarction, n (%)	390 (28.4)	309 (22.9)
Mean creatinine clearance, mL/min (SD)	77.2 (29.9)	78.8 (29.6)
Mean CHA_2DS_2–VASc (SD)	3.6 (1.6)	3.6 (1.5)
Mean HAS-BLED (SD)*	2.7 (0.7)	2.7 (0.7)
OAC treatment naïve at baseline, n (%)†	1021 (74.3)	775 (57.4)
Drug-eluting stent only, n (%)	1099 (79.9)	1152 (85.4)

*Modified. †<14 days of consecutive OAC treatment. NB: presented data are regardless of treatment with dabigatran or warfarin; data were not available for 1 patient. ACS, acute coronary syndrome; AF, atrial fibrillation; OAC, oral anticoagulant; SD, standard deviation.

Bleeding events: ACS vs non-ACS

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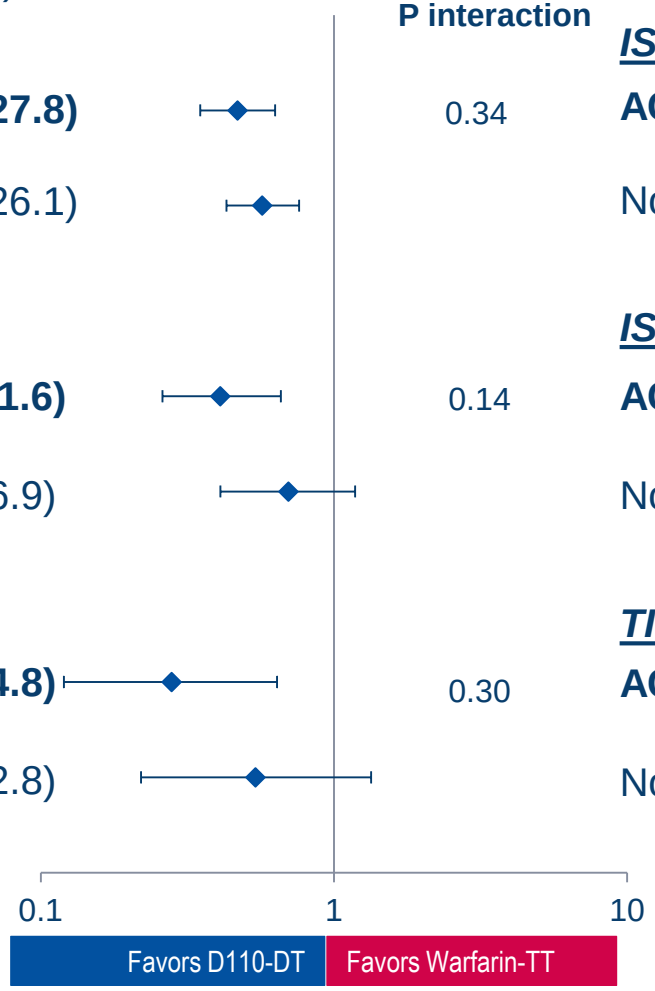
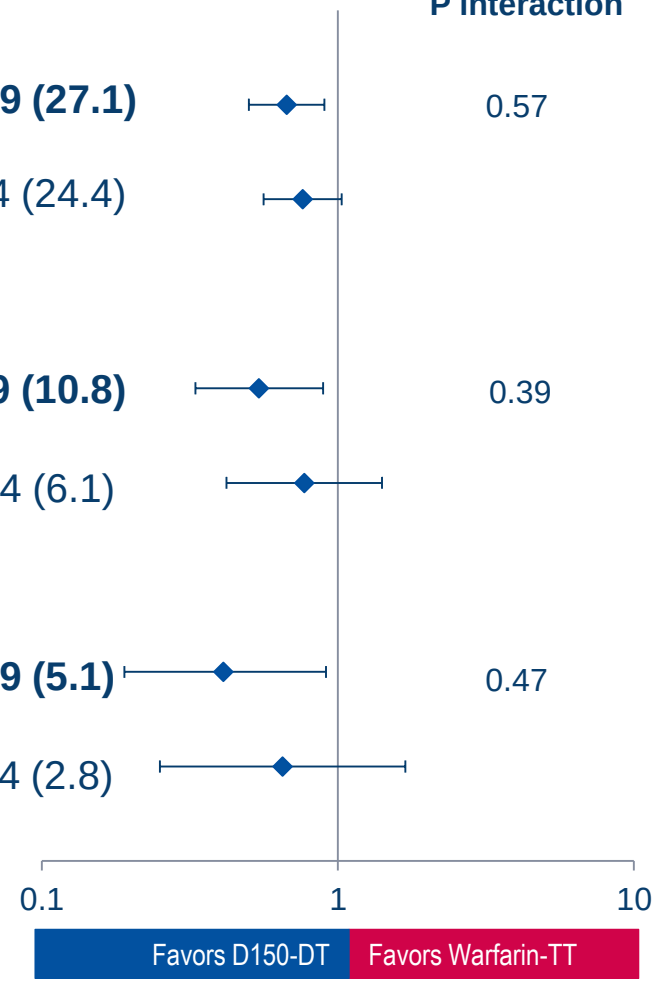
Study in NVAF patients undergoing PCI

	D110-DT n/N (%)	Warfarin-TT n/N (%)	P interaction
ISTH Major/CRNM Bleeding			
ACS	**75/509 (14.7)**	**132/475 (27.8)**	0.34
Non-ACS	76/472 (16.1)	132/505 (26.1)	
ISTH Major Bleeding			
ACS	**26/509 (5.1)**	**55/475 (11.6)**	0.14
Non-ACS	23/472 (4.9)	35/505 (6.9)	
TIMI Major Bleeding			
ACS	**7/509 (1.4)**	**23/475 (4.8)**	0.30
Non-ACS	7/472 (1.5)	14/505 (2.8)	



	D150-DT n/N (%)	Warfarin-TT n/N (%)	P interaction
ISTH Major/CRNM Bleeding			
ACS	**80/391 (20.5)**	**100/369 (27.1)**	0.57
Non-ACS	74/372 (19.9)	96/394 (24.4)	
ISTH Major Bleeding			
ACS	**25/391 (6.4)**	**40/369 (10.8)**	0.39
Non-ACS	18/372 (4.8)	24/394 (6.1)	
TIMI Major Bleeding			
ACS	**9/391 (2.3)**	**19/369 (5.1)**	0.47
Non-ACS	7/372 (1.9)	11/394 (2.8)	

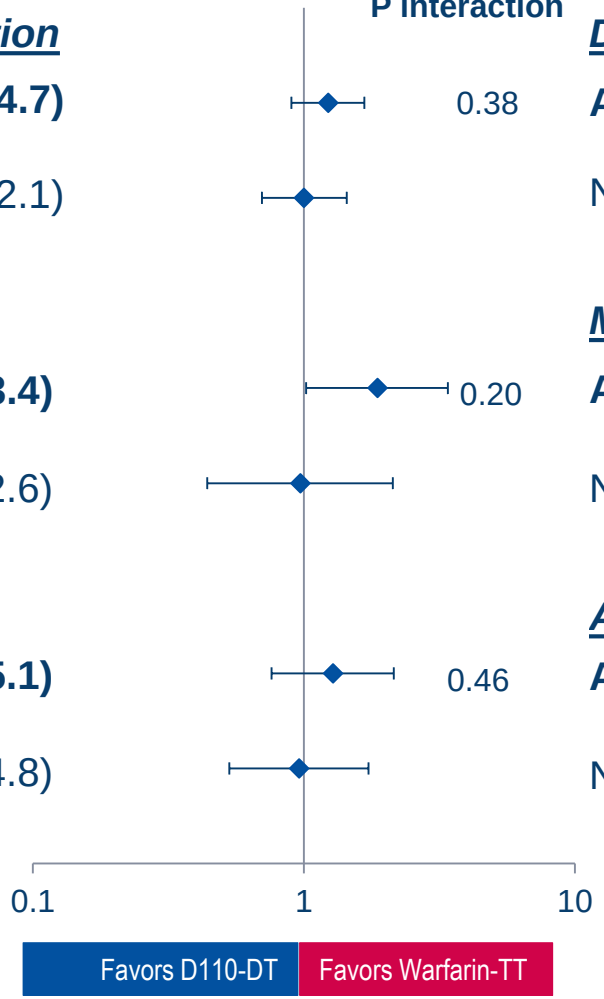


ACS, acute coronary syndrome; CRNM, clinically relevant non-major; D, dabigatran; DT, dual therapy; ISTH, International Society on Thrombosis and Haemostasis; TIMI, thrombolysis in myocardial infarction; TT, triple therapy.

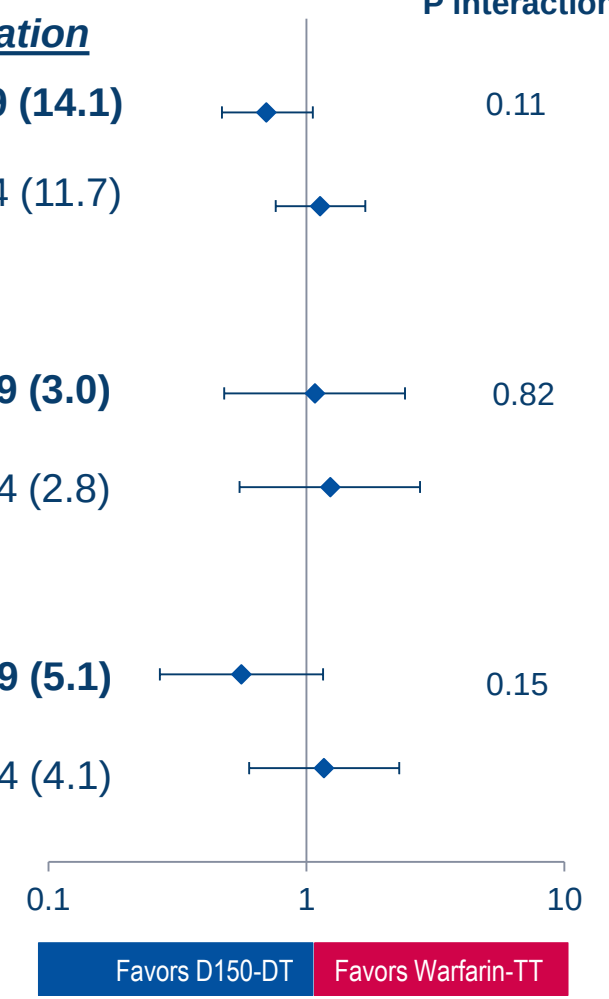
Death and thromboembolic events: ACS vs non-ACS

RE-DUAL PCI
Study in NVAF patients undergoing PCI

	D110-DT n/N (%)	Warfarin-TT n/N (%)	P interaction
DTE or Unplanned Revascularization			
ACS	**92/509 (18.1)**	**70/475 (14.7)**	0.38
Non-ACS	57/472 (12.1)	61/505 (12.1)	
Myocardial Infarction			
ACS	**32/509 (6.3)**	**16/475 (3.4)**	0.20
Non-ACS	12/472 (2.5)	13/505 (2.6)	
All-cause Death			
ACS	**34/509 (6.7)**	**24/475 (5.1)**	0.46
Non-ACS	21/472 (4.4)	24/505 (4.8)	



	D150-DT n/N (%)	Warfarin-TT n/N (%)	P interaction
DTE or Unplanned Revascularization			
ACS	**41/391 (10.5)**	**52/369 (14.1)**	0.11
Non-ACS	49/372 (13.2)	46/394 (11.7)	
Myocardial Infarction			
ACS	**13/391 (3.3)**	**11/369 (3.0)**	0.82
Non-ACS	13/372 (3.5)	11/394 (2.8)	
All-cause Death			
ACS	**12/391 (3.1)**	**19/369 (5.1)**	0.15
Non-ACS	18/372 (4.8)	16/394 (4.1)	



ACS, acute coronary syndrome; D, dabigatran; DT, dual therapy; DTE, death or thromboembolic event (myocardial infarction, stroke or systemic embolism); TT, triple therapy.

BMS vs DES: baseline characteristics

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Study in NVAF patients undergoing PCI

	BMS (N=404)	DES (N=2251)
Mean age, years (SD)	70.1 (9.2)	71.0 (8.6)
Male, n (%)	289 (71.5)	1729 (76.8)
Atrial fibrillation at baseline, n (%)		
Paroxysmal	182 (45.0)	1139 (50.6)
Persistent	61 (15.1)	411 (18.3)
Permanent	160 (39.6)	701 (31.1)
Diabetes, n (%)	136 (33.7)	827 (36.7)
Prior stroke, n (%)	36 (8.9)	186 (8.3)
Prior myocardial infarction, n (%)	112 (27.7)	568 (25.2)
Mean creatinine clearance, mL/min (SD)	79.4 (28.1)	77.7 (30.1)
Mean CHA_2DS_2–VASc (SD)	3.7 (1.6)	3.6 (1.5)
Mean HAS-BLED (SD)*	2.7 (0.7)	2.7 (0.7)
OAC treatment naïve at baseline, n (%)†	292 (72.3)	1456 (64.7)
Acute coronary syndrome, n (%)	239 (59.2)	1099 (48.8)

*Modified. †<14 days of consecutive OAC treatment. NB: presented data are regardless of treatment with dabigatran or warfarin; data were not available for 8 patients and are not included for 62 patients with other stent or both BMS and DES. BMS, bare-metal stent; DES, drug-eluting stent; OAC, oral anticoagulant; SD, standard deviation.

Bleeding events: BMS vs DES

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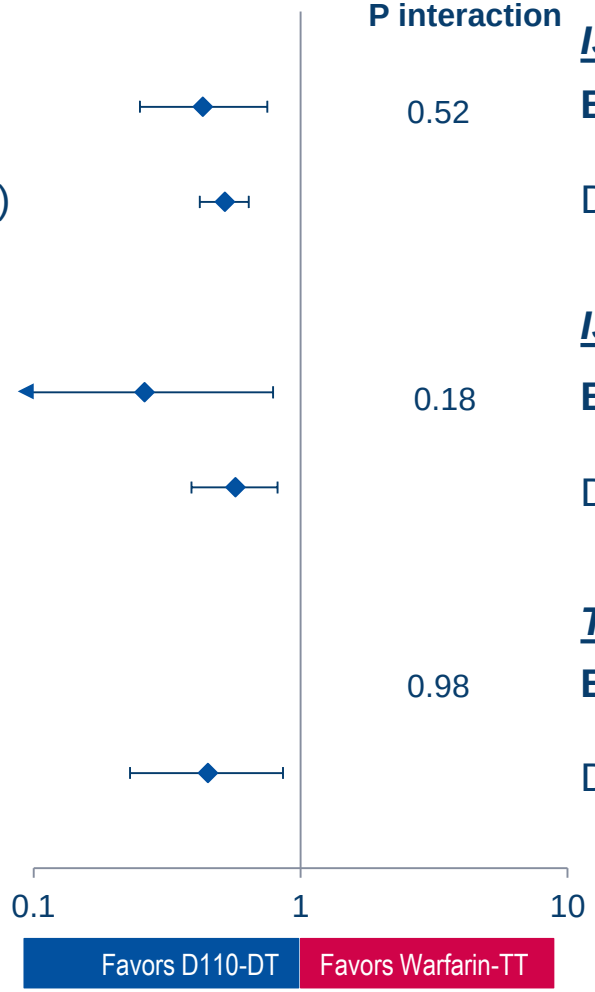
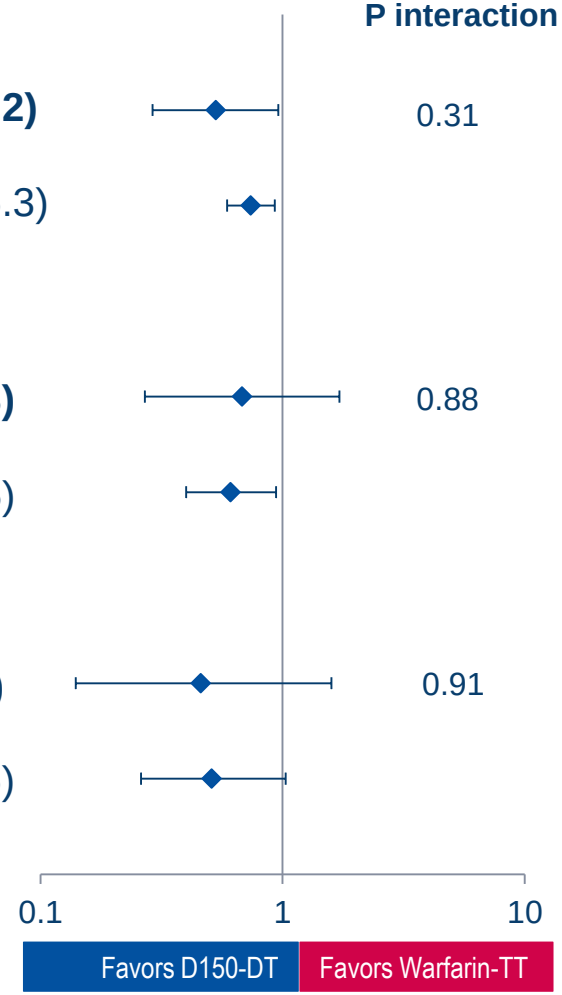
Study in NVAF patients undergoing PCI

	D110-DT n/N (%)	Warfarin-TT n/N (%)	P interaction
ISTH Major/CRNM Bleeding			
BMS	**19/148 (12.8)**	**35/133 (26.3)**	0.52
DES	127/804 (15.8)	288/826 (27.6)	
ISTH Major Bleeding			
BMS	**4/148 (2.7)**	**13/133 (9.8)**	0.18
DES	44/804 (5.5)	77/826 (9.3)	
TIMI Major Bleeding			
BMS	**0/148 (0.0)**	**8/133 (6.0)**	0.98
DES	13/804 (1.6)	29/826 (3.5)	



	D150-DT n/N (%)	Warfarin-TT n/N (%)	P interaction
ISTH Major/CRNM Bleeding			
BMS	**18/123 (14.6)**	**27/107 (25.2)**	0.31
DES	133/621 (21.4)	168/638 (26.3)	
ISTH Major Bleeding			
BMS	**8/123 (6.5)**	**10/107 (9.3)**	0.88
DES	34/621 (5.5)	54/638 (8.5)	
TIMI Major Bleeding			
BMS	**4/123 (3.3)**	**7/107 (6.5)**	0.91
DES	12/621 (1.9)	23/638 (3.6)	

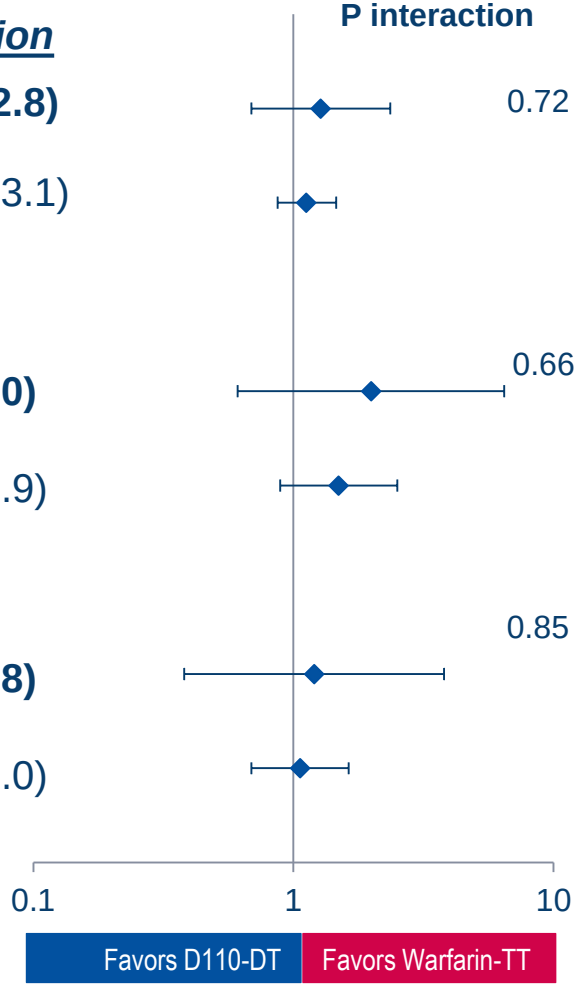


BMS, bare-metal stent; CRNM, clinically relevant non-major; D, dabigatran; DES, drug-eluting stent; DT, dual therapy; ISTH, International Society on Thrombosis and Haemostasis; TIMI, thrombolysis in myocardial infarction; TT, triple therapy.

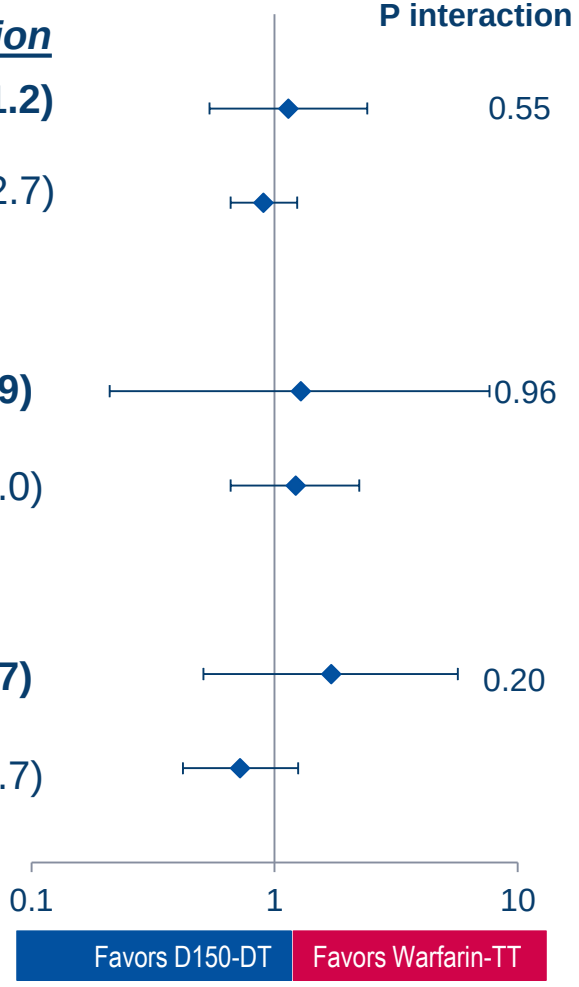
Death and thromboembolic events: BMS vs DES

RE-DUAL PCI
Study in NVAF patients undergoing PCI

	D110 dual-DT n/N (%)	Warfarin-TT n/N (%)	P interaction
DTE or Unplanned Revascularization			
BMS	**25/148 (16.9)**	**17/133 (12.8)**	0.72
DES	118/804 (14.7)	108/826 (13.1)	
Myocardial Infarction			
BMS	**9/148 (6.1)**	**4/133 (3.0)**	0.66
DES	35/804 (4.4)	24/826 (2.9)	
All-cause Death			
BMS	**7/148 (4.7)**	**5/133 (3.8)**	0.85
DES	43/804 (5.3)	41/826 (5.0)	



	D150-DT n/N (%)	Warfarin-TT n/N (%)	P interaction
DTE or Unplanned Revascularization			
BMS	**16/123 (13.0)**	**12/107 (11.2)**	0.55
DES	73/621 (11.8)	81/638 (12.7)	
Myocardial Infarction			
BMS	**3/123 (2.4)**	**2/107 (1.9)**	0.96
DES	23/621 (3.7)	19/638 (3.0)	
All-cause Death			
BMS	**8/123 (6.5)**	**4/107 (3.7)**	0.20
DES	22/621 (3.5)	30/638 (4.7)	



BMS, bare-metal stent; D, dabigatran; DES, drug-eluting stent; DT, dual therapy; DTE, death or thromboembolic event (myocardial infarction, stroke or systemic embolism); TT, triple therapy.

Ticagrelor/clopidogrel: baseline characteristics

RE-DUAL PCI
Study in NVAF patients undergoing PCI

	Ticagrelor* (N=327)	Clopidogrel† (N=2398)
Mean age, years (SD)	69.7 (9.6)	70.9 (8.5)
Male, n (%)	253 (77.4)	1817 (75.8)
Atrial fibrillation at baseline, n (%)		
Paroxysmal	185 (56.6)	1166 (48.6)
Persistent	53 (16.2)	431 (18.0)
Permanent	88 (26.9)	800 (33.4)
Diabetes, n (%)	123 (37.6)	870 (36.3)
Prior stroke, n (%)	20 (6.1)	206 (8.6)
Prior myocardial infarction, n (%)	91 (27.8)	608 (25.4)
Mean creatinine clearance, mL/min (SD)	80.5 (32.2)	77.7 (29.4)
Mean CHA_2DS_2-VASc (SD)	3.4 (1.6)	3.6 (1.6)
Mean HAS-BLED (SD)**	2.6 (0.7)	2.7 (0.7)
OAC treatment at baseline, n (%)		
Long-term	78 (23.9)	851 (35.5)
Treatment naïve‡	249 (76.1)	1547 (64.5)

*58 patients who received ticagrelor + clopidogrel are included in the ticagrelor subgroup; †93 patients who received neither clopidogrel nor ticagrelor are included in the clopidogrel subgroup.
**Modified. ‡<14 days of consecutive OAC treatment. NB: presented data are regardless of treatment with dabigatran or warfarin. OAC, oral anticoagulant; SD, standard deviation.

Ticagrelor/clopidogrel: baseline characteristics

RE-DUAL PCI
Study in NVAF patients undergoing PCI

	Ticagrelor* (N=327)	Clopidogrel† (N=2398)
Indication for PCI, n (%)		
Stable angina/positive stress test	78 (23.9)	1104 (46.0)
Acute coronary syndrome	240 (73.4)	1135 (47.3)
Staged procedure or other	70 (21.4)	562 (23.4)
Stent type, n (%)		
DES only	275 (84.1)	1976 (82.4)
BMS only	40 (12.2)	364 (15.2)
DES and BMS, or other	11 (3.4)	51 (2.1)
DAPT trial complexity factors, n (%)‡		
No clinical/procedural factor	67 (20.5)	941 (39.2)
Clinical complexity factor	193 (59.0)	981 (40.9)
Procedural complexity factor	16 (4.9)	254 (10.6)
Both clinical and procedural complexity factors	51 (15.6)	222 (9.3)

*58 patients who received ticagrelor + clopidogrel are included in the ticagrelor subgroup; †93 patients who received neither clopidogrel nor ticagrelor are included in the clopidogrel subgroup.
NB: presented data are regardless of treatment with dabigatran or warfarin. BMS, bare-metal stent; DES, drug-eluting stent. ‡Mauri et al. Am Heart J. 2010;160:1035-1041.

Time to first ISTH major or CRNM bleeding event in relation to ticagrelor or clopidogrel

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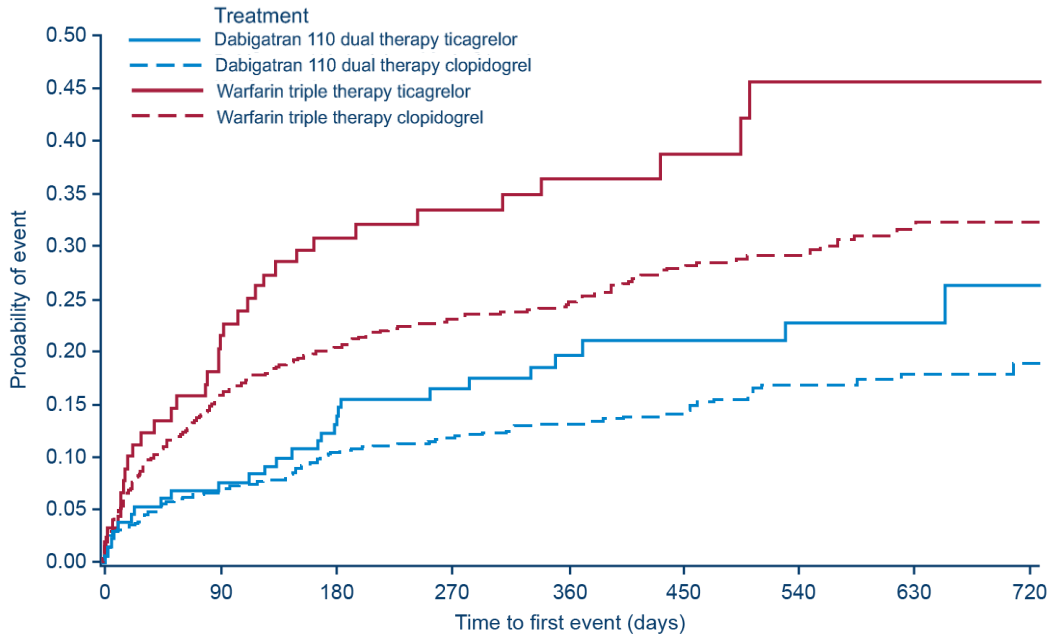
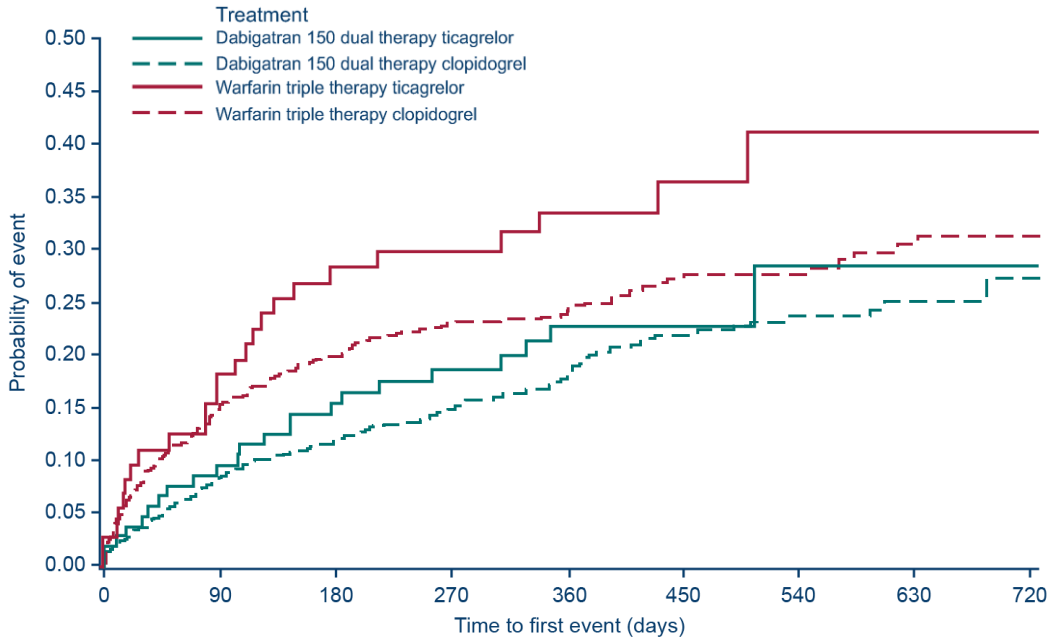
Dabigatran 110 dual therapy



Patients at risk					
Dabigatran 110 dual therapy ticagrelor	132	110	67	39	15
Dabigatran 110 dual therapy clopidogrel	847	721	478	223	76
Warfarin triple therapy ticagrelor	91	56	36	13	5
Warfarin triple therapy clopidogrel	866	646	407	185	58

Dabigatran 150 dual therapy



Patients at risk					
Dabigatran 150 dual therapy ticagrelor	104	85	50	22	6
Dabigatran 150 dual therapy clopidogrel	650	548	343	155	58
Warfarin triple therapy ticagrelor	73	47	30	11	4
Warfarin triple therapy clopidogrel	673	501	311	136	43

Full analysis set presented. HRs and Wald CIs from Cox proportional-hazard model. For the dabigatran 110 vs warfarin comparison, the model is stratified by age, non-elderly vs elderly (<70 or ≥70 years in Japan and <80 or ≥80 years old elsewhere). For the dabigatran 150 vs warfarin comparison, an unstratified model is used, elderly patients outside the United States are excluded. Non-inferiority P value is one sided (alpha=0.025). Wald two-sided P value from (stratified) Cox proportional-hazard model (alpha=0.05).
CI, confidence interval; CRNM, clinically relevant non-major; HR, hazard ratio; ISTH, International Society on Thrombosis and Haemostasis.

Bleeding events: ticagrelor/clopidogrel

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Study in NVAF patients undergoing PCI

	D110-DT n/N (%)	Warfarin-TT n/N (%)	P (interaction)
ISTH Major/CRNM Bleeding			
Ticagrelor*	**28/132 (21.2)**	**34/91 (37.4)**	0.69
Clopidogrel†	123/849 (14.5)	230/890 (25.8)	
ISTH Major Bleeding			
Ticagrelor*	**11/132 (8.3)**	**15/91 (16.5)**	0.75
Clopidogrel†	38/849 (4.5)	75/890 (8.4)	
TIMI Major Bleeding			
Ticagrelor*	**3/132 (2.3)**	**9/91 (9.9)**	0.39
Clopidogrel†	11/849 (1.3)	28/890 (3.1)	

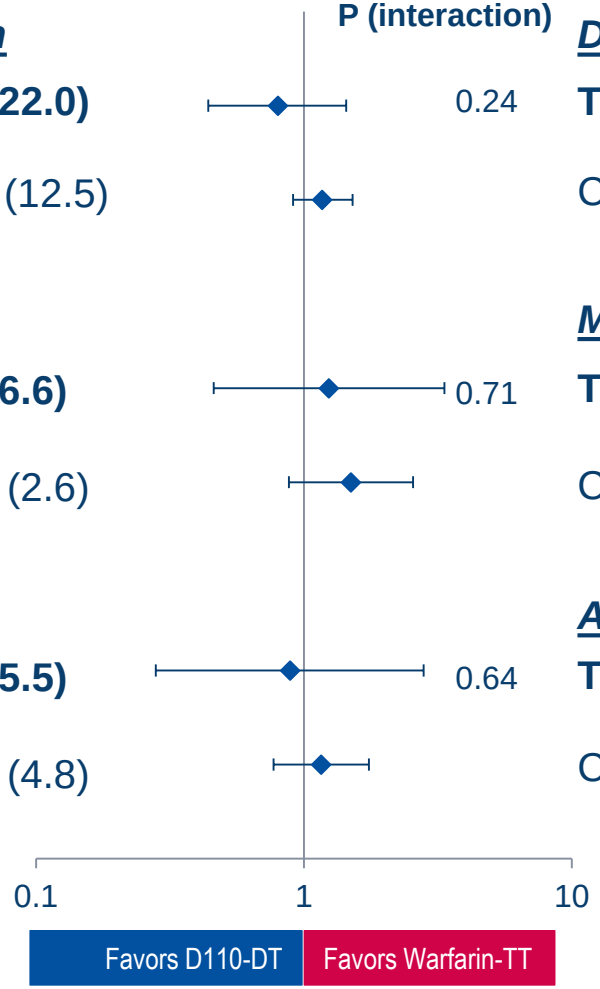
	D150-DT n/N (%)	Warfarin-TT n/N (%)	P (interaction)
ISTH Major/CRNM Bleeding			
Ticagrelor*	**24/104 (23.1)**	**25/73 (34.2)**	0.53
Clopidogrel†	130/659 (19.7)	171/691 (24.7)	
ISTH Major Bleeding			
Ticagrelor*	**8/104 (7.7)**	**12/73 (16.4)**	0.37
Clopidogrel†	35/659 (5.3)	52/691 (7.5)	
TIMI Major Bleeding			
Ticagrelor*	**2/104 (1.9)**	**7/73 (9.6)**	0.17
Clopidogrel†	14/659 (2.1)	23/691 (3.3)	

*58 patients who received ticagrelor + clopidogrel are included in the ticagrelor subgroup; †93 patients who received neither clopidogrel nor ticagrelor are included in the clopidogrel subgroup.
CRNM, clinically relevant non-major; D, dabigatran; DT, dual therapy ISTH, International Society on Thrombosis and Haemostasis; TIMI, thrombolysis in myocardial infarction; TT, triple therapy.

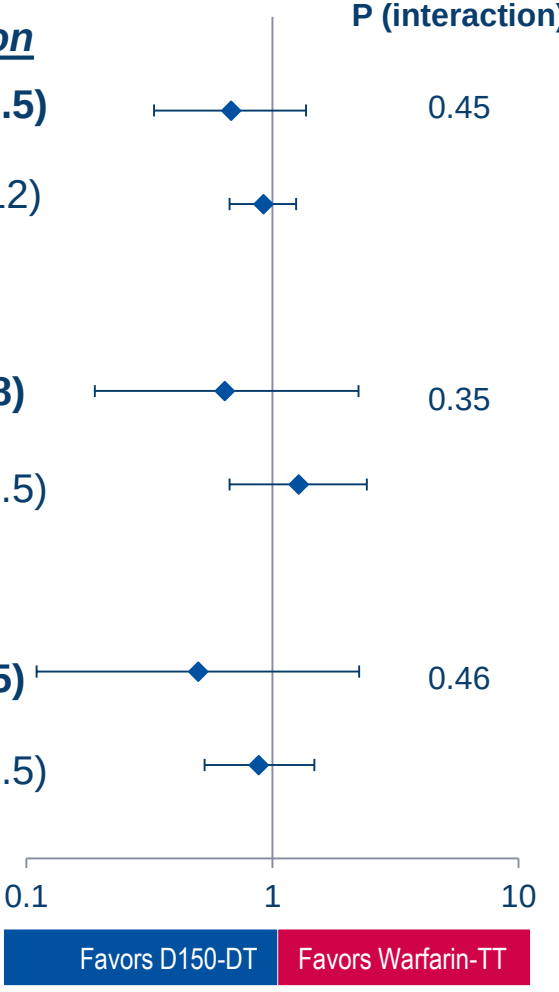
Death and thromboembolic events: ticagrelor/clopidogrel

RE-DUAL PCI
Study in NVAF patients undergoing PCI

	D110-DT n/N (%)	Warfarin-TT n/N (%)	P (interaction)
DTE or Unplanned Revascularization			
Ticagrelor*	**25/132 (18.9)**	**20/91 (22.0)**	0.24
Clopidogrel†	124/849 (14.6)	111/890 (12.5)	
Myocardial Infarction			
Ticagrelor*	**11/132 (8.3)**	**6/91 (6.6)**	0.71
Clopidogrel†	33/849 (3.9)	23/890 (2.6)	
All-cause Death			
Ticagrelor*	**7/132 (5.3)**	**5/91 (5.5)**	0.64
Clopidogrel†	48/849 (5.7)	43/890 (4.8)	



	D150-DT n/N (%)	Warfarin-TT n/N (%)	P (interaction)
DTE or Unplanned Revascularization			
Ticagrelor*	**16/104 (15.4)**	**15/73 (20.5)**	0.45
Clopidogrel†	74/659 (11.2)	83/691 (12)	
Myocardial Infarction			
Ticagrelor*	**5/104 (4.8)**	**5/73 (6.8)**	0.35
Clopidogrel†	21/659 (3.2)	17/691 (2.5)	
All-cause Death			
Ticagrelor*	**3/104 (2.9)**	**4/73 (5.5)**	0.46
Clopidogrel†	27/659 (4.1)	31/691 (4.5)	



*58 patients who received ticagrelor + clopidogrel are included in the ticagrelor subgroup; †93 patients who received neither clopidogrel nor ticagrelor are included in the clopidogrel subgroup. D, dabigatran, DT, dual therapy; DTE, death or thromboembolic event (myocardial infarction, stroke or systemic embolism); TT, triple therapy.

Summary

RE-DUAL PCI
Study in NVAF patients undergoing PCI

In the RE-DUAL PCI trial

- The index indication for PCI was an ACS in 50% of the patients
- DES alone were used in 83% of the patients, similarly in patients with ACS and non-ACS
- The majority of patients received clopidogrel; 12% of the patients received ticagrelor either as part of dabigatran dual therapy or warfarin triple therapy
- Patients who received ticagrelor more often had ACS as the index event, were oral anticoagulation naïve, and had DAPT clinical complexity factors; and ticagrelor was associated with higher bleeding risk than clopidogrel
- There were no significant interactions in any of the presented outcomes for any of the presented subgroups

ACS, acute coronary syndrome; DAPT, dual antiplatelet therapy; DES, drug-eluting stent; PCI, percutaneous coronary intervention.

Conclusions

RE-DUAL PCI
Study in NVAF patients undergoing PCI

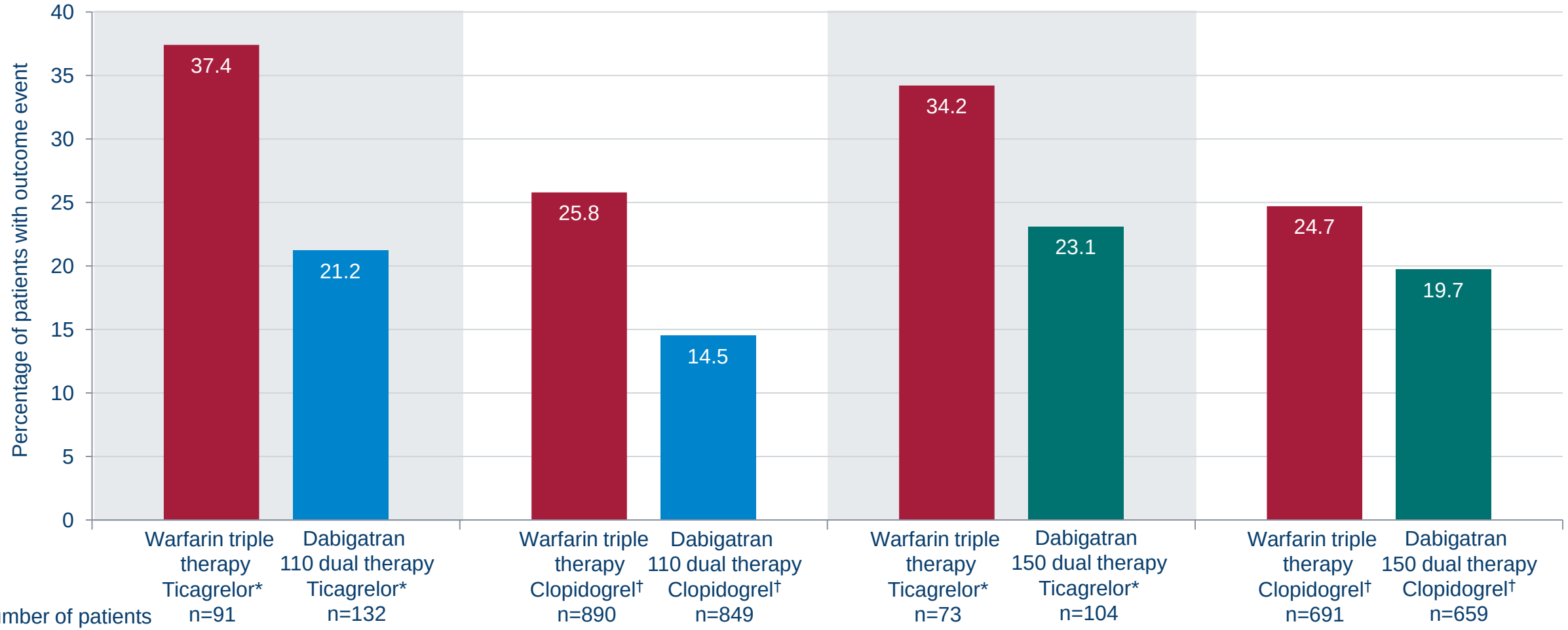
The benefit of the dabigatran dual therapy versus warfarin triple therapy in patients with atrial fibrillation who underwent PCI was consistent with the main results in:

- patients with ACS and non-ACS at index event
- those receiving DES or BMS
- patients treated with the P2Y12 inhibitors ticagrelor or clopidogrel

ACS, acute coronary syndrome; BMS, bare-metal stent; DES, drug-eluting stent; PCI, percutaneous coronary intervention.

ISTH major or clinically relevant non-major bleeding event in relation to P2Y12 inhibition

RE-DUAL PCI
Study in NVAF patients undergoing PCI



*58 patients who received ticagrelor + clopidogrel are included in the ticagrelor subgroup; †93 patients who received neither clopidogrel nor ticagrelor are included in the clopidogrel subgroup.
ISTH, International Society on Thrombosis and Haemostasis.

ACS vs non-ACS: baseline characteristics

RE-DUAL PCI
Study in NVAF patients undergoing PCI

	ACS		Non-ACS		ACS		Non-ACS	
	Dabigatran 110 dual therapy (n=509)	Warfarin triple therapy (n=475)	Dabigatran 110 dual therapy (n=472)	Warfarin triple therapy (n=505)	Dabigatran 150 dual therapy (n=391)	Warfarin triple therapy* (n=369)	Dabigatran 150 dual therapy (n=372)	Warfarin triple therapy* (n=394)
Mean age, years (SD)	71.7 (9.7)	72.5 (8.9)	71.4 (7.9)	71.0 (8.8)	68.1 (8.1)	69.4 (7.6)	69.1 (7.2)	68.3 (7.7)
Male, n (%)	362 (71.1)	356 (74.9)	366 (77.5)	393 (77.8)	292 (74.7)	288 (78.0)	300 (80.6)	305 (77.4)
AF at baseline, n (%)								
Paroxysmal	267 (52.5)	234 (49.3)	220 (46.6)	250 (49.5)	207 (52.9)	182 (49.3)	173 (46.5)	194 (49.2)
Persistent	89 (17.5)	80 (16.8)	85 (18.0)	98 (19.4)	60 (15.3)	67 (18.2)	72 (19.4)	82 (20.8)
Permanent	153 (30.1)	161 (33.9)	167 (35.4)	157 (31.1)	123 (31.5)	120 (32.5)	127 (34.1)	118 (29.9)
Diabetes, n (%)	191 (37.5)	167 (35.2)	171 (36.2)	204 (40.4)	134 (34.3)	135 (36.6)	126 (33.9)	168 (42.6)
Prior stroke, n (%)	42 (8.3)	42 (8.8)	32 (6.8)	58 (11.5)	22 (5.6)	33 (8.9)	30 (8.1)	44 (11.2)
Prior MI, n (%)	146 (28.7)	140 (29.5)	91 (19.3)	128 (25.3)	104 (26.6)	106 (28.7)	90 (24.2)	105 (26.6)
Mean CrCl, mL/min (SD)	76.0 (30.6)	72.8 (25.9)	76.5 (27.0)	77.8 (31.6)	84.2 (32.2)	78.6 (26.0)	83.1 (29.7)	83.8 (32.3)
Mean CHA_2DS_2−VASc (SD)	3.8 (1.7)	3.8 (1.5)	3.6 (1.5)	3.8 (1.5)	3.3 (1.5)	3.6 (1.5)	3.3 (1.5)	3.6 (1.5)
Mean HAS-BLED (SD)†	2.7 (0.7)	2.8 (0.7)	2.7 (0.7)	2.8 (0.8)	2.6 (0.7)	2.7 (0.8)	2.6 (0.7)	2.7 (0.8)
OAC treatment at baseline, n (%)								
Long-term‡	**138 (27.1)**	**124 (26.1)**	**209 (44.3)**	**210 (41.6)**	**92 (23.5)**	**87 (23.6)**	**155 (41.7)**	**156 (39.6)**
Treatment naïve	**371 (72.9)**	**351 (73.9)**	**263 (55.7)**	**295 (58.4)**	**299 (76.5)**	**282 (76.4)**	**217 (58.3)**	**238 (60.4)**
Stent type, n (%)								
DES only	401 (78.8)	389 (81.9)	403 (85.4)	437 (86.5)	309 (79.0)	299 (81.0)	312 (83.9)	339 (86.0)
BMS only	92 (18.1)	76 (16.0)	56 (11.9)	57 (11.3)	71 (18.2)	61 (16.5)	52 (14.0)	46 (11.7)

*For the comparison with dabigatran 150 dual therapy, elderly patients outside the United States are excluded. †Modified. ‡≥14 days of consecutive OAC treatment. NB: The treatment group pairs with a >10% difference in ACS vs non-ACS are in bold. ACS, acute coronary syndrome; AF, atrial fibrillation; BMS, bare-metal stent; CrCl, creatinine clearance; DES, drug-eluting stent; MI, myocardial infarction; OAC, oral anticoagulant; SD, standard deviation.

BMS vs DES at baseline: baseline characteristics

RE-DUAL PCI
Study in NVAF patients undergoing PCI

	BMS		DES		BMS		DES	
	Dabigatran 110 dual therapy (n=148)	Warfarin triple therapy (n=133)	Dabigatran 110 dual therapy (n=804)	Warfarin triple therapy (n=826)	Dabigatran 150 dual therapy (n=123)	Warfarin triple therapy* (n=107)	Dabigatran 150 dual therapy (n=621)	Warfarin triple therapy* (n=638)
Mean age, years (SD)	70.9 (9.6)	72.0 (9.1)	71.7 (8.8)	71.8 (8.9)	67.0 (8.2)	69.2 (7.7)	68.9 (7.5)	68.8 (7.7)
Male, n (%)	107 (72.3)	92 (69.2)	600 (74.6)	639 (77.4)	90 (73.2)	77 (72.0)	490 (78.9)	500 (78.4)
AF at baseline, n (%)								
Paroxysmal	**60 (40.5)**	67 (50.4)	**417 (51.9)**	403 (48.8)	55 (44.7)	56 (52.3)	319 (51.4)	309 (48.4)
Persistent	25 (16.9)	16 (12.0)	142 (17.7)	159 (19.2)	20 (16.3)	15 (14.0)	110 (17.7)	131 (20.5)
Permanent	**63 (42.6)**	50 (37.6)	**245 (30.5)**	264 (32.0)	47 (38.2)	36 (33.6)	192 (30.9)	198 (31.0)
Diabetes, n (%)	57 (38.5)	39 (29.3)	292 (36.3)	321 (38.9)	40 (32.5)	**30 (28.0)**	214 (34.5)	**263 (41.2)**
Prior stroke, n (%)	14 (9.5)	16 (12.0)	59 (7.3)	83 (10.0)	6 (4.9)	13 (12.1)	44 (7.1)	63 (9.9)
Prior MI, n (%)	42 (28.4)	34 (25.6)	188 (23.4)	229 (27.7)	36 (29.3)	27 (25.2)	151 (24.3)	180 (28.2)
Mean CrCl, mL/min (SD)	77.2 (26.9)	75.4 (28.5)	76.0 (29.3)	75.1 (29.1)	86.2 (28.1)	81.1 (28.7)	83.4 (31.7)	81.0 (29.7)
Mean CHA_2DS_2−VASc (SD)	3.8 (1.6)	3.9 (1.5)	3.7 (1.6)	3.8 (1.5)	3.4 (1.5)	3.7 (1.5)	3.3 (1.5)	3.6 (1.5)
Mean HAS-BLED (SD)†	2.7 (0.7)	2.9 (0.7)	2.7 (0.7)	2.8 (0.8)	2.5 (0.7)	2.8 (0.7)	2.6 (0.7)	2.7 (0.8)
OAC treatment at baseline, n (%)								
Long-term‡	41 (27.7)	36 (27.1)	296 (36.8)	294 (35.6)	35 (28.5)	31 (29.0)	205 (33.0)	208 (32.6)
Treatment naïve	107 (72.3)	97 (72.9)	508 (63.2)	532 (64.4)	88 (71.5)	76 (71.0)	416 (67.0)	430 (67.4)
Indication for PCI, n (%)								
Stable angina/positive stress test	59 (39.9)	50 (37.6)	363 (45.1)	371 (44.9)	45 (36.6)	**38 (35.5)**	268 (43.2)	**294 (46.1)**
ACS	**92 (62.2)**	**76 (57.1)**	**401 (49.9)**	**389 (47.1)**	71 (57.7)	**61 (57.0)**	309 (49.8)	**299 (46.9)**

*For the comparison with dabigatran 150 dual therapy, elderly patients outside the United States are excluded. †Modified. ‡≥14 days of consecutive OAC treatment. NB: The treatment group pairs with a >10% difference in BMS vs DES are in bold. ACS, acute coronary syndrome; AF, atrial fibrillation; BMS, bare-metal stent; CrCl, creatinine clearance; DES, drug-eluting stent; MI, myocardial infarction; OAC, oral anticoagulant; SD, standard deviation; PCI, percutaneous coronary intervention.

Ticagrelor/clopidogrel: baseline characteristics

RE-DUAL PCI
Study in NVAF patients undergoing PCI

	Ticagrelor*		Clopidogrel†		Ticagrelor*		Clopidogrel†	
	Dabigatran 110 dual therapy (n=132)	Warfarin triple therapy (n=91)	Dabigatran 110 dual therapy (n=849)	Warfarin triple therapy (n=890)	Dabigatran 150 dual therapy (n=104)	Warfarin triple therapy‡ (n=73)	Dabigatran 150 dual therapy (n=659)	Warfarin triple therapy‡ (n=691)
Mean age, years (SD)	71.0 (9.5)	71.0 (9.5)	71.6 (8.8)	71.8 (8.8)	67.0 (9.2)	68.1 (8.0)	68.9 (7.4)	68.9 (7.6)
Male, n (%)	96 (72.7)	76 (83.5)	632 (74.4)	674 (75.7)	81 (77.9)	62 (84.9)	511 (77.5)	532 (77.0)
AF at baseline, n (%)								
Paroxysmal	73 (55.3)	46 (50.5)	414 (48.8)	438 (49.2)	**66 (63.5)**	37 (50.7)	**314 (47.6)**	339 (49.1)
Persistent	24 (18.2)	12 (13.2)	150 (17.7)	166 (18.7)	17 (16.3)	11 (15.1)	115 (17.5)	138 (20.0)
Permanent	35 (26.5)	33 (36.3)	285 (33.6)	285 (32.0)	**20 (19.2)**	25 (34.2)	**230 (34.9)**	213 (30.8)
Diabetes, n (%)	50 (37.9)	32 (35.2)	312 (36.7)	339 (38.1)	41 (39.4)	28 (38.4)	219 (33.2)	275 (39.8)
Prior stroke, n (%)	8 (6.1)	7 (7.7)	66 (7.8)	93 (10.4)	5 (4.8)	6 (8.2)	47 (7.1)	71 (10.3)
Prior MI, n (%)	37(28.0)	28 (30.8)	200 (23.6)	240 (27.0)	26 (25.0)	23 (31.5)	168 (25.5)	188 (27.2)
Mean CrCl, mL/min (SD)	77.1 (32.2)	74.9 (29.0)	76.1 (28.3)	75.4 (29.1)	89.4 (33.1)	81.3 (28.6)	82.7 (30.6)	81.3 (29.7)
Mean CHA_2DS_2-VASc (SD)	3.5 (1.7)	3.7 (1.5)	3.7 (1.6)	3.8 (1.5)	3.1 (1.5)	3.4 (1.4)	3.3 (1.5)	3.6 (1.6)
Mean HAS-BLED (SD)**	2.6 (0.7)	2.8 (0.6)	2.7 (0.7)	2.8 (0.7)	2.5 (0.7)	2.7 (0.7)	2.6 (0.7)	2.7 (0.8)
OAC treatment at baseline, n (%)								
Long-term††	**29 (22.0)**	25 (27.5)	**318 (37.5)**	310 (34.8)	**24 (23.1)**	17 (23.3)	**223 (33.8)**	227 (32.9)
Treatment naïve	**103 (78.0)**	66 (72.5)	**531 (62.5)**	580 (65.2)	**80 (76.9)**	56 (76.7)	**436 (66.2)**	464 (67.1)

*58 patients who received ticagrelor + clopidogrel are included in the ticagrelor subgroup; †93 patients who received neither clopidogrel nor ticagrelor are included in the clopidogrel subgroup. ‡For the comparison with dabigatran 150 dual therapy, elderly patients outside the United States are excluded. **Modified. ††≥14 days of consecutive OAC treatment. NB: The treatment group pairs with a >10% difference in clopidogrel vs ticagrelor are in bold. AF, atrial fibrillation; CrCl, creatinine clearance; MI, myocardial infarction; OAC, oral anticoagulant; SD, standard deviation.

Ticagrelor/clopidogrel: baseline characteristics

RE-DUAL PCI
Study in NVAF patients undergoing PCI

	Ticagrelor*		Clopidogrel†		Ticagrelor*		Clopidogrel†	
	Dabigatran 110 dual therapy (n=132)	Warfarin triple therapy (n=91)	Dabigatran 110 dual therapy (n=849)	Warfarin triple therapy (n=890)	Dabigatran 150 dual therapy (n=104)	Warfarin triple therapy‡ (n=73)	Dabigatran 150 dual therapy (n=659)	Warfarin triple therapy‡ (n=691)
Indication for PCI, n (%)								
Stable angina/positive stress test	**30 (22.7)**	**25 (27.5)**	**403 (47.5)**	**404 (45.4)**	**23 (22.1)**	**22 (30.1)**	**297 (45.1)**	**317 (45.9)**
Acute coronary syndrome	**101 (76.5)**	**61 (67.0)**	**408 (48.1)**	**414 (46.5)**	**78 (75.0)**	**48 (65.8)**	**313 (47.5)**	**321 (46.5)**
Staged procedure or other	26 (19.7)	16 (17.6)	173 (20.4)	214 (24.0)	28 (26.9)	12 (16.4)	175 (26.6)	172 (24.9)
Stent type, n (%)								
DES only	113 (85.6)	77 (84.6)	691 (81.4)	749 (84.2)	85 (81.7)	61 (83.6)	536 (81.3)	577 (83.5)
BMS only	14 (10.6)	12 (13.2)	134 (15.8)	121 (13.6)	14 (13.5)	10 (13.7)	109 (16.5)	97 (14.0)
DES and BMS, or other	4 (3.0)	2 (2.2)	23 (2.7)	15 (1.7)	5 (4.8)	2 (2.7)	13 (2.0)	12 (1.7)
Dual antiplatelet treatment factor, n (%)								
No clinical/procedural factor	**26 (19.7)**	**21 (23.1)**	**327 (38.5)**	**360 (40.4)**	**20 (19.2)**	**17 (23.3)**	**254 (38.5)**	**288 (41.7)**
Clinical complexity factor	**77 (58.3)**	**48 (52.7)**	**348 (41.0)**	**366 (41.1)**	**68 (65.4)**	**39 (53.4)**	**267 (40.5)**	**287 (41.5)**
Procedural complexity factor	5 (3.8)	6 (6.6)	88 (10.4)	91 (10.2)	5 (4.8)	5 (6.8)	75 (11.4)	61 (8.8)
Both clinical and procedural complexity factors	24 (18.2)	16 (17.6)	86 (10.1)	73 (8.2)	11 (10.6)	12 (16.4)	63 (9.6)	55 (8.0)

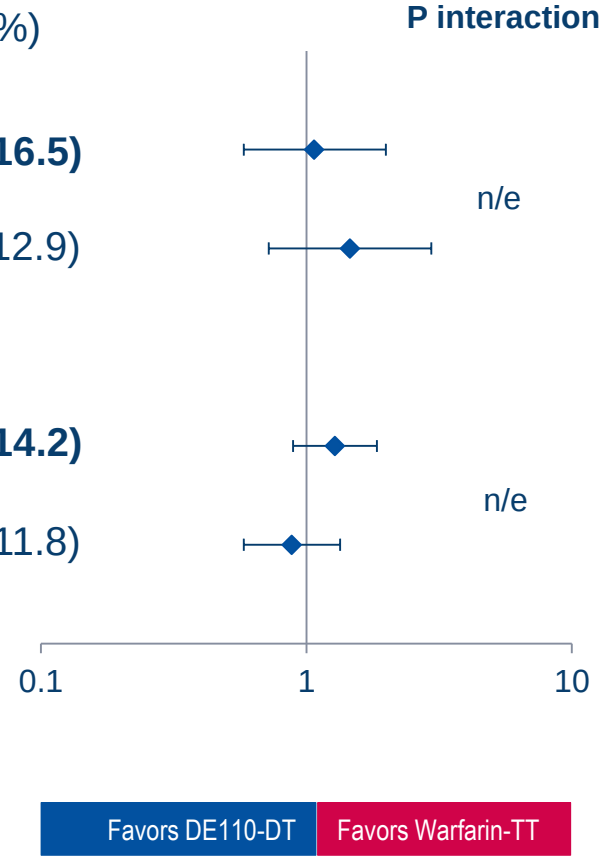
*58 patients who received ticagrelor + clopidogrel are included in the ticagrelor subgroup; †93 patients who received neither clopidogrel nor ticagrelor are included in the clopidogrel subgroup.

‡For the comparison with dabigatran 150 dual therapy, elderly patients outside the United States are excluded; NB: The treatment group pairs with a >10% difference in clopidogrel vs ticagrelor are in bold. BMS, bare-metal stent; DES, drug-eluting stent; PCI, percutaneous coronary intervention.

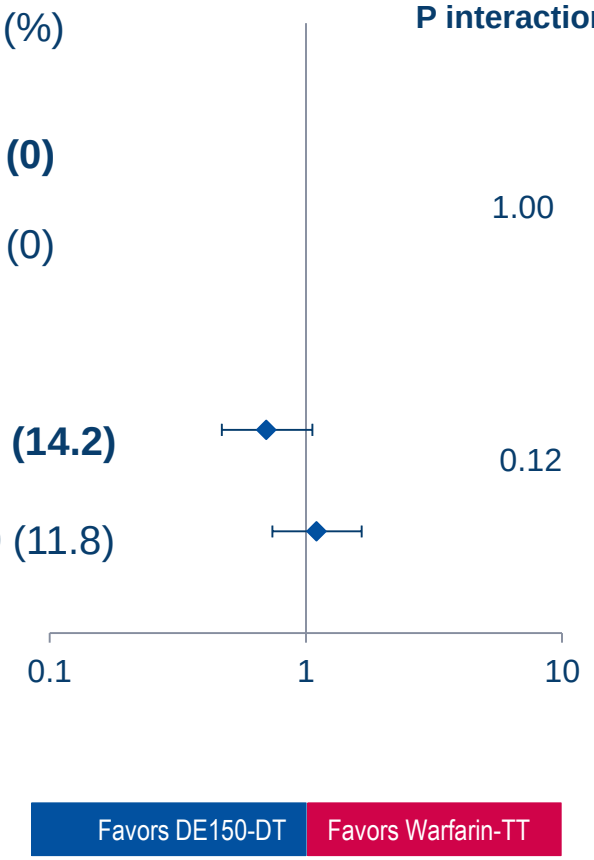
DTE or unplanned revascularization: ACS/non-ACS
Elderly & non-elderly

RE-DUAL PCI
Study in NVAF patients undergoing PCI

	D110-DT n/N (%)	Warfarin-TT n/N (%)
Elderly		
ACS	**23/133 (17.3)**	**18/109 (16.5)**
Non-ACS	16/92 (17.4)	15/116 (12.9)
Non-elderly		
ACS	**69/376 (18.4)**	**52/366 (14.2)**
Non-ACS	41/380 (10.8)	46/389 (11.8)



	D150-DT n/N (%)	Warfarin-TT n/N (%)
Elderly		
ACS	**0/3 (0)**	**0/3 (0)**
Non-ACS	1/5 (20.0)	0/5 (0)
Non-elderly		
ACS	**41/388 (10.6)**	**52/366 (14.2)**
Non-ACS	48/367 (13.1)	46/389 (11.8)

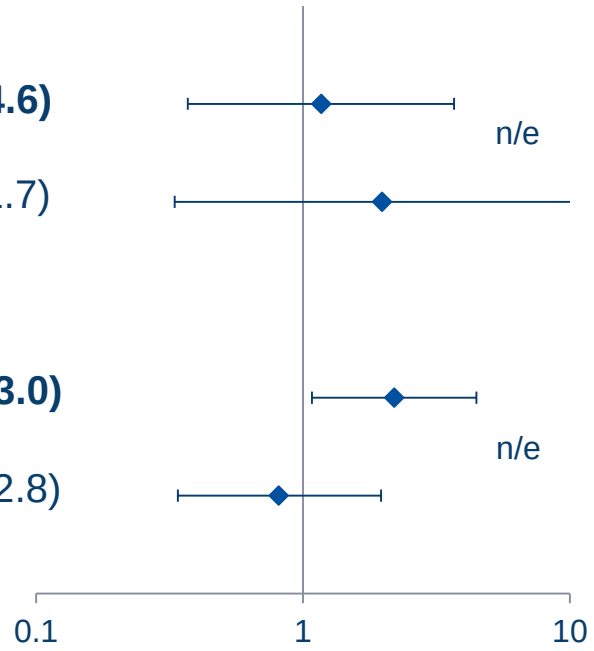


ACS, acute coronary syndrome; D, dabigatran; DT, dual therapy; DTE, death or thromboembolic event (myocardial infarction, stroke or systemic embolism); n/e, non-evaluable; TT, triple therapy.

Myocardial infarction: ACS/non-ACS
Elderly & non-elderly

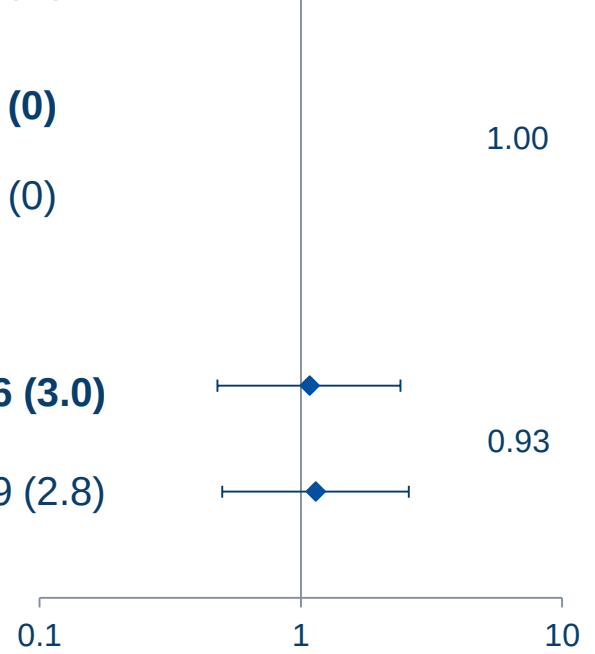
RE-DUAL PCI
Study in NVAF patients undergoing PCI

	D110-DT n/N (%)	Warfarin-TT n/N (%)	P interaction
Elderly			
ACS	**7/133 (5.3)**	**5/109 (4.6)**	n/e
Non-ACS	3/92 (3.3)	2/116 (1.7)	
Non-elderly			
ACS	**25/376 (6.6)**	**11/366 (3.0)**	n/e
Non-ACS	9/380 (2.4)	11/389 (2.8)	



Favors DE110-DT | Favors Warfarin-TT

	D150-DT n/N (%)	Warfarin-TT n/N (%)	P interaction
Elderly			
ACS	**0/3 (0)**	**0/3 (0)**	1.00
Non-ACS	1/5 (20.0)	0/5 (0)	
Non-elderly			
ACS	**13/388 (3.4)**	**11/366 (3.0)**	0.93
Non-ACS	12/367 (3.3)	11/389 (2.8)	



Favors DE150-DT | Favors Warfarin-TT

ACS, acute coronary syndrome; D, dabigatran; DT, dual therapy; n/e, non-evaluable; TT, triple therapy.