Approaches to Stroke prevention in patients with Atrial Fibrillation Nuances and Updates

Department of Cardiology

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Luis Garcia MD, FHRS
Clinical Cardiac Electrophysiologist

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Atrial Fibrillation- Stroke/TIA prevention

Medications(Anticoagulants)

Left atrial appendage occlusion(Watchman)

1. Female Sex and CHA2Ds2 VASC

2. NOAC (CKD, HD)

3. Focus on post PCI and Afib

CHAD2-Vasc score- Female sex- Impact

Risk factors	Score	CHADS2-VASc score and Annual stroke risk (%)
Congestive heart failure	1	Score 1 = 1.3
Hypertension	1	2 = 2.2
Age > 75 years	2	3 = 3.2
Diabetes mellitus	1	4 = 4
Stroke/TIA/systemic embolism	2	5 = 6.7
Vascular disease	1	6 = 9.8
Age 65 to 74 years	1	7 = 9.6
Sex (female)	1	8 = 6.7
		9 = 15.2

Camm et al 2010, ESC guidelines

Question #1

A 49 yo year old healthy woman with well controlled Hypertension has paroxysmal Afib twice this year noted on a 2 week event monitor. She has no other medical problems and is healthy.

Based on the recent guidelines from ACC/AHA for CVA prevention, is an anticoagulant recommended (ie NOAC/Warfarin)?

1. YES
2. NO
3. Not sure

Question #2

What is her CHA2DS2 Vasc score

1. 1
2. 2

AFIB anticoagulation guidelines (female sex)

Revised

Level 1- Evidence A

For patients with AF, oral anticoagulants are recommended in:

1. **CHA2DS2-VASc score 3 or greater in women(<65yo)**
2. **CHA2DS2-VASc score of 2 or greater in men**

Camm et al Circulation. 2019 Jul 9;140(2):e125-e151.

Impact of Female sex and Cha2ds2vasc score

-Observational cohort study using data from 3 Danish nationwide registries in Denmark

-A total of 337 769 patients with incident AF were identified between January 1997 and December 2015.

- Outcomes were obtained through monitoring databases

(1) 1 year of follow-up

(2) 5 years of follow-up

Female vs. Male thromboembolism risk using CHA2DS2 vasc

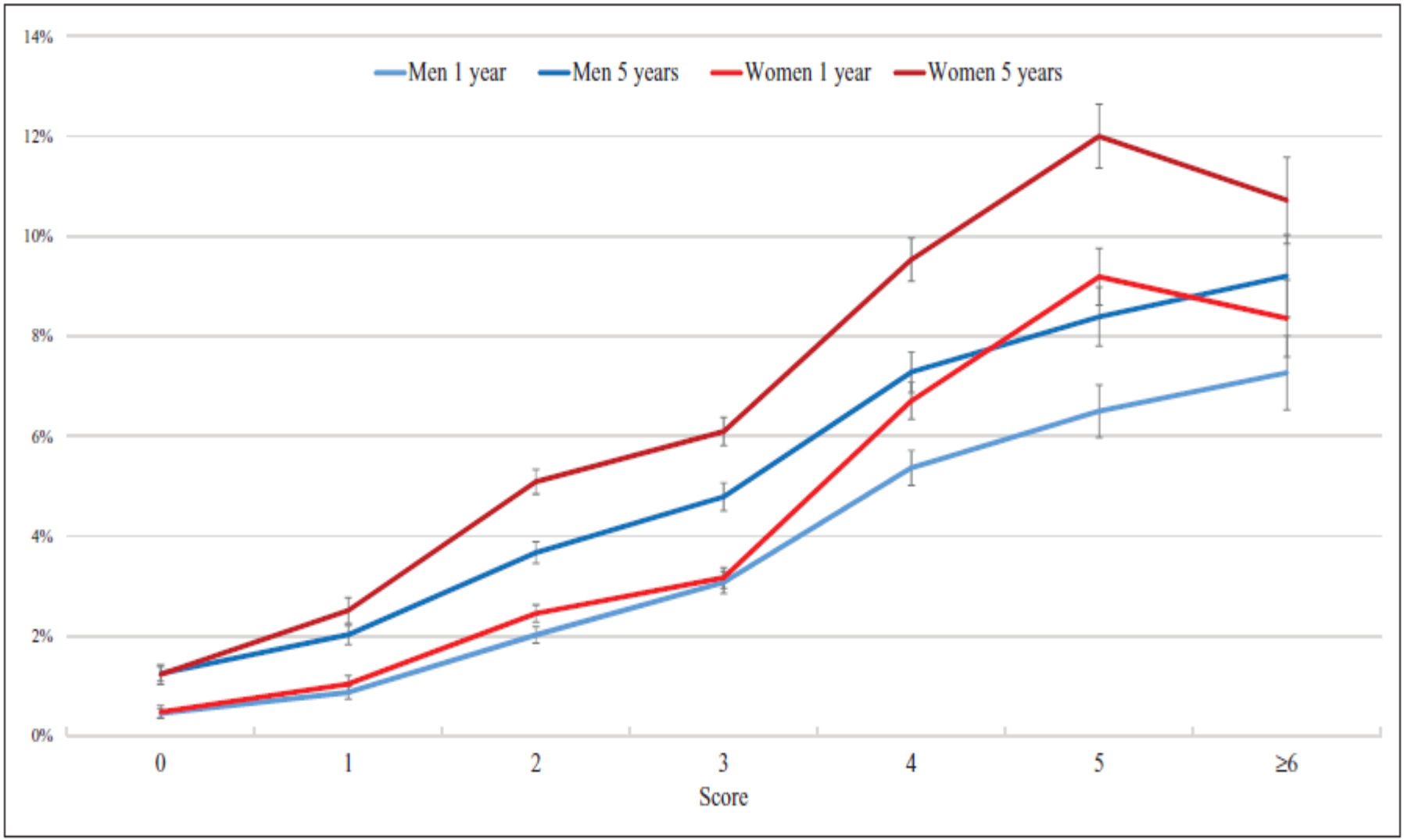


Figure 2. Absolute risk of thromboembolism among men (blue) and women (red).
Risks are assessed at 1 and 5 years of follow-up.

Nielsen et al, Circulation. 2018 Feb 20;137(8):832-840.

Impact

- **Women <65 yo and Afib have NO further risk of thromboembolism vs. men**

-(This cohort→Changed the guidelines)

- **Women who have one other CHADSvasc risk factors are at a greater risk of thromboembolism vs. men**

(in general)

Female Sex impact on CVA/TIA is age dependent

Adding female sex to the CHA2DS2-VASc score matters for:

1. **Age >65 years or**

2. **≥2 non–sex-related stroke risk factors**

(Women < 65 yo)

Anticoagulants and CKD

NOAC and Kidney Dysfunction

Apixaban- (serum creatinine ≥1.5 mg/dL), age ≥80 years or weight ≤60kg

Dabigatran- CrCl 15 to 30 mL/min,

Rivaroxaban- CrCl ≤50mL/min,

Edoxaban- Edoxaban is not approved for (CrCl <30 mL/ min) or (CrCl >95 mL/min).

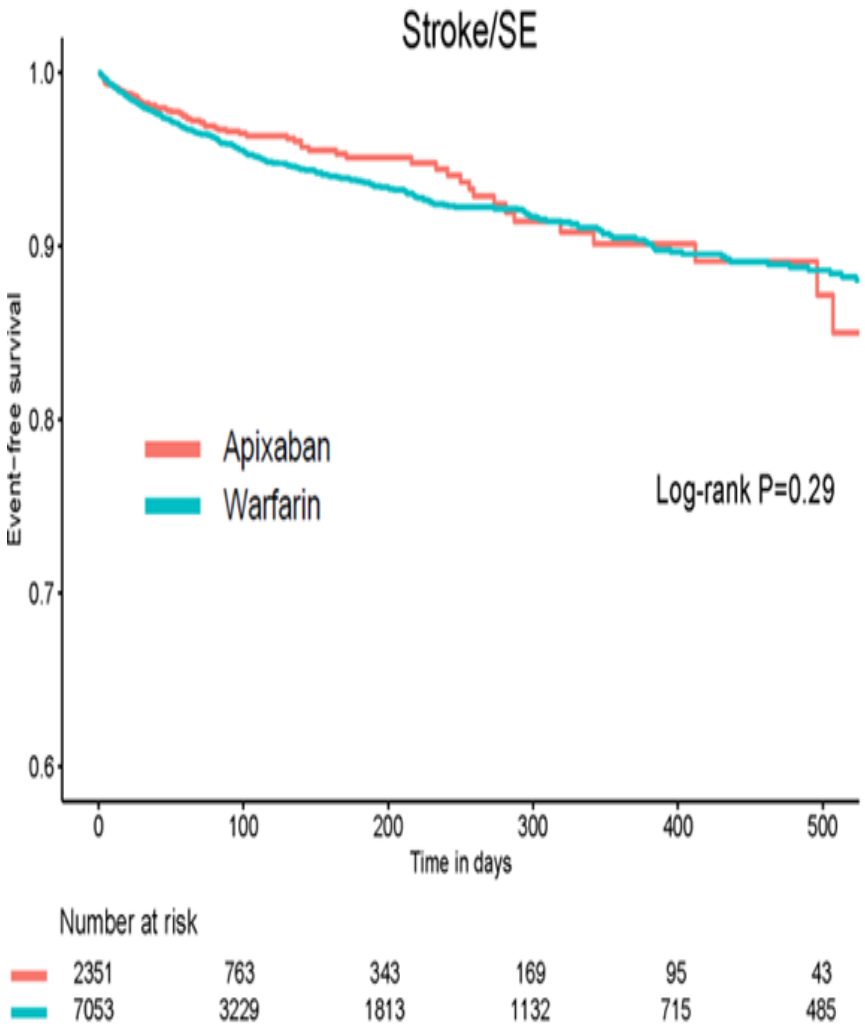
January et al 2019 AHA/ACC/HRS Focused Update of the 2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation

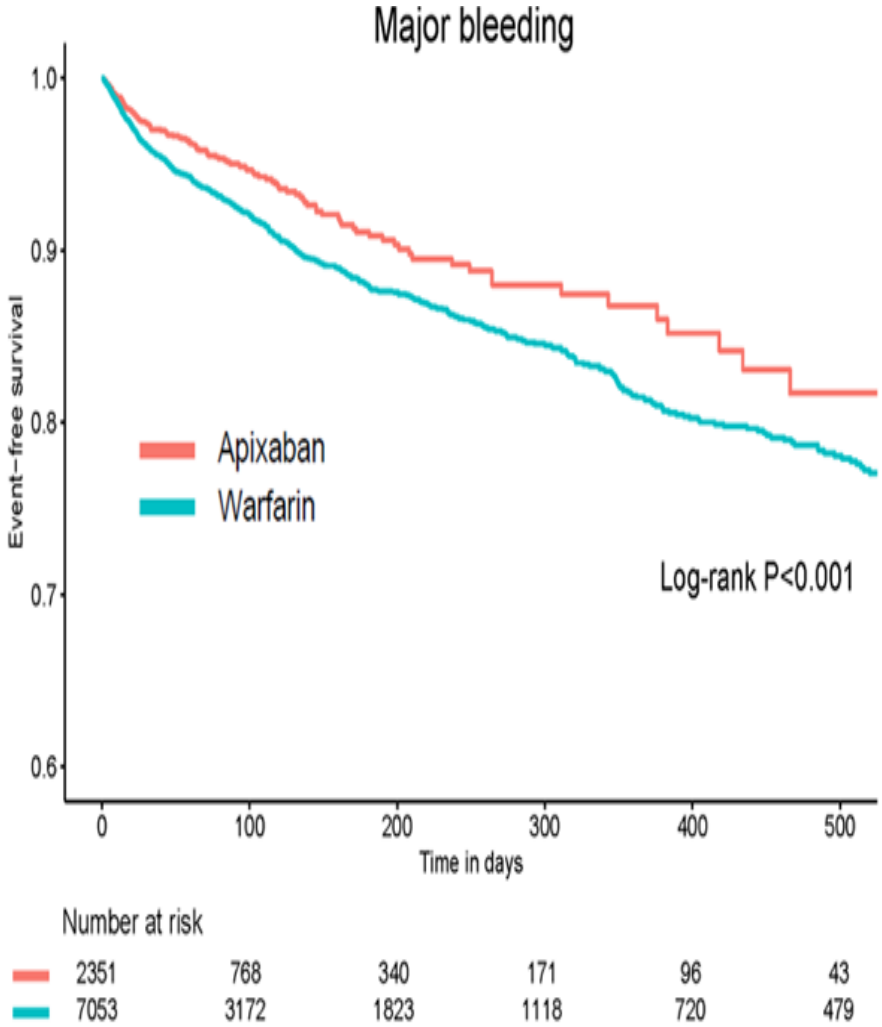
AC and ESRD/HD

- Apixiban most tested- (2.5mg BID elevated level in HD pts)
- All Retrospective data-
- Small studies have suggested no increase in bleeding and similar bleeding rates (apixiban vs. warfarin)
- Largest Data set- Medicare population- retrospective review

Reed et al Res Pract Thromb Haemost. 2018 Apr; 2(2): 291–298, Stanton et alPharmacotherapy. 2017 Apr;37(4):412-419.

Apixiban vs. warfarin in HD population





Other Anticoagulants

1. Rivaroxaban and Dabigatran- One Large review

Fresenius Medical Care North America (FMCNA) ESRD database

Dabigatran and Rivaroxaban-

Increased bleeding events vs. warfarin- Not recommended

2. Edoxaban- It is not recommended in patients with endstage renal disease or on dialysis.

Chan Circulation. 2015 Mar 17;131(11):972-9

AFIB, PCI and Antithrombotic therapy

Atrial Fibrillation and PCI

- Approximately 20–30% of ischemic strokes are related to AF, associated with increased risk of heart failure, cardiovascular morbidity, and mortality
- Approximately 3 million patients undergo percutaneous coronary intervention (PCI) each year worldwide
- For patients undergoing PCI, approximately 5–10% have concomitant AF or other indications for long-term oral anticoagulant (OAC) therapy
- Typically Patient undergoing PCI(received Dual anti-platelet therapy) receive DAPT for 3-6 month post intervention and >1 year in some patients

1. D.J. Angiolillo, et al ,Circ. Cardiovasc. Interv. 9 (2016) e004395.

AFIB and PCI(Dual Diagnosis)

- Initially patients post PCIand AFib received:
  DAPT and AC

- **RISK: Significant increase in Bleeding**

- **WOEST trial- PCI pts (Triple vs. Dual)**

- **Warfarin/ASA vs. Warfarin/DAPT**

1. *Significant Bleeding/ Transfusions with Warfarin/DAPT

2. No increased risk of Thrombotic events with Warfarin/clopidogrel

Dewilde et al Lancet 2013

AFIB and PCI(Dual Diagnosis)

Newer trials

ISAR-TRIPLE- 6weeks vs. 6months of Triple therapy

No increased thrombotic events in **6 week group**

No increased Bleeding in **6 month group**

--- 6 weeks maybe enough!

Fieldler et Jacc 2015

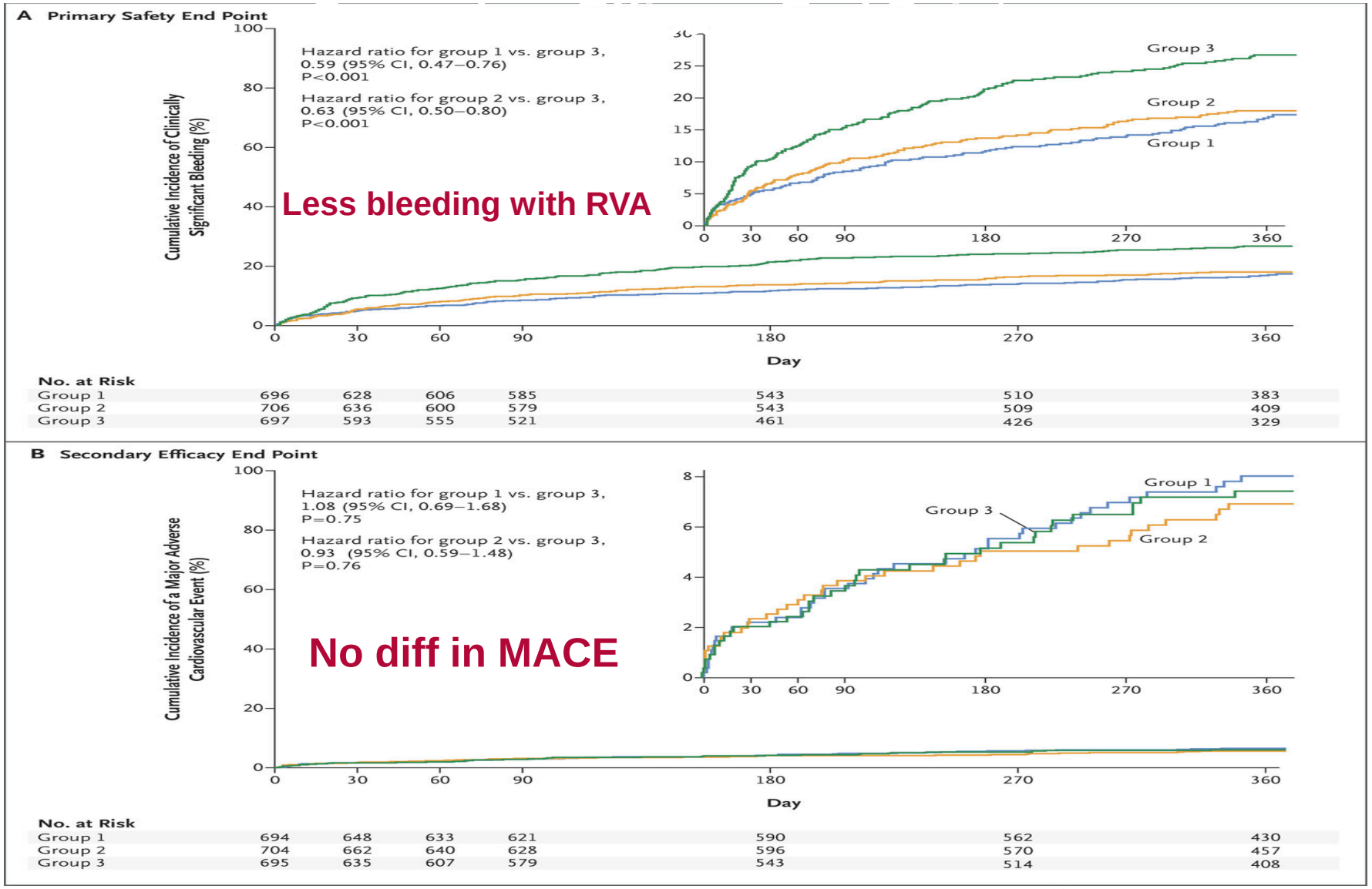
AFIB and PCI(Dual diagnosis)

PIONEER AF-PCI TRIAL- Rivaroxaban(RVA) and (Mono-Anti-Platelet MAPT)

1. **RVA 15mg QD/MAPT -12 months**
2. **RVA 2.5mg BID/DAPT- 1, 6, 12 months- converted to MAPT**
3. **Warfarin DAPT- 1, 6, 12 months- converted to MAPT**

N Engl J Med. 2016 Dec 22;375(25):2423-2434.

Pioneer- AF-PCI –More bleeding with Triple therapy



Gibson CM et al. N Engl J Med 2016;375:2423-2434.

Primary Safety End Point/Duration of therapy

Table 2. Cumulative Incidence of the Primary Safety End Point and Its Components, with Stratification According to Intended Duration of DAPT.*

Cohort and End Point	Group 1	Group 2	Groups 1 and 2	Group 3	Group 1 vs. Group 3		Group 2 vs. Group 3		Groups 1 and 2 vs. Group 3	
	No. of Participants with Events (Kaplan–Meier Event Rate)				Hazard Ratio (95% CI)	P Value	Hazard Ratio (95% CI)	P Value	Hazard Ratio (95% CI)	P Value
All participants — no.	696	706	1402	697						
Participants assigned to DAPT for 6 mo — no.		248		243						
Clinically significant bleeding		39 (17.5)		68 (31.2)			0.51 (0.34–0.75)	<0.001		
Major bleeding		7 (3.3)		9 (4.4)			0.74 (0.28–2.00)	0.56		
Minor bleeding		1 (0.5)		6 (2.9)			0.16 (0.02–1.32)	0.05		
Bleeding requiring medical attention		32 (14.5)		56 (26.0)			0.51 (0.33–0.79)	0.002		
Participants assigned to DAPT for 12 mo — no.		350		341						
Clinically significant bleeding		59 (17.9)		72 (23.9)			0.74 (0.52–1.04)	0.08		
Major bleeding		4 (1.3)		6 (2.1)			0.60 (0.17–2.14)	0.43		
Minor bleeding		5 (1.5)		5 (1.8)			0.91 (0.26–3.14)	0.88		
Bleeding requiring medical attention		52 (15.9)		62 (20.9)			0.75 (0.52–1.09)	0.13		

1. RVA MAPT or low RVA DAPT

2. No obvious signal of harm with Short term triple therapy

Gibson CM et al. N Engl J Med 2016;375:2423-2434.

Dabigatran and Apixiban Me too…

RE-DUAL PCI

Dabigatran/MAPT vs. Warfarin/DAPT

--Bleeding events less with Dabigatran 15% vs Warfarin 26%

--Thrombotic events non inferior

AUGUSTUS Apixiban-

Bleeding events:

1. Warfarin/DAPT (18.7%)
2. Apixaban/DAPT(13.8%)
3. VKA/MAPT (10.9%)
4. Apixaban/MAPT **(7.3%)**

Entrust- Edoxaban

1. Edoxoban 17%
2. Warfarin 20%

Non inferior

Cannon et NEJM 2017, Lopes et al NEJM 2019

NOAC and Anti-platelet therapy

NOACs and DAPT-

1. Appears to reliably reduce bleeding events
2. Thrombotic events do not appear to be increased
3. Short term triple therapy or Dual therapy seems reasonable
4. No Large Gross signals of harm, unclear if there are patient specific factors that may contribute to utilizing triple therapy

Conclusion

Lots of new DATA!

- **--Women <65 yo, recommendations similar to men**

- **--NOAC can be given in renal failure**

1. **Doses should be adjusted in CKD**
2. **Apixiban some safety data 5mg Bid?**

- **Anticoagulants and MAPT becoming standard of care**

THANK YOU!