Impact of Low-dose Rivaroxaban plus Aspirin on Myocardial Infarction in Patients with Peripheral Artery Disease with and without Concomitant Coronary Artery Disease: Insights from VOYAGER PAD

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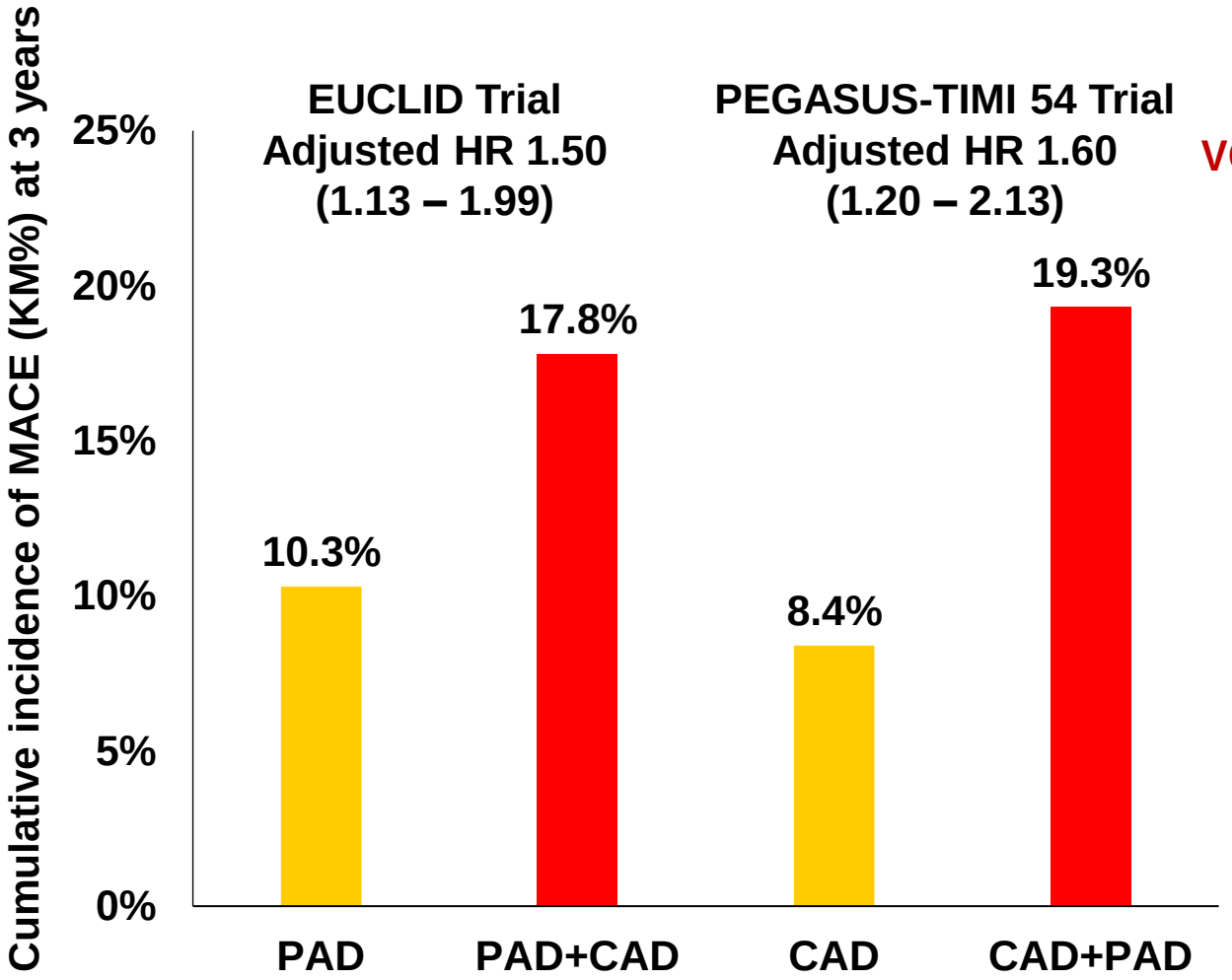
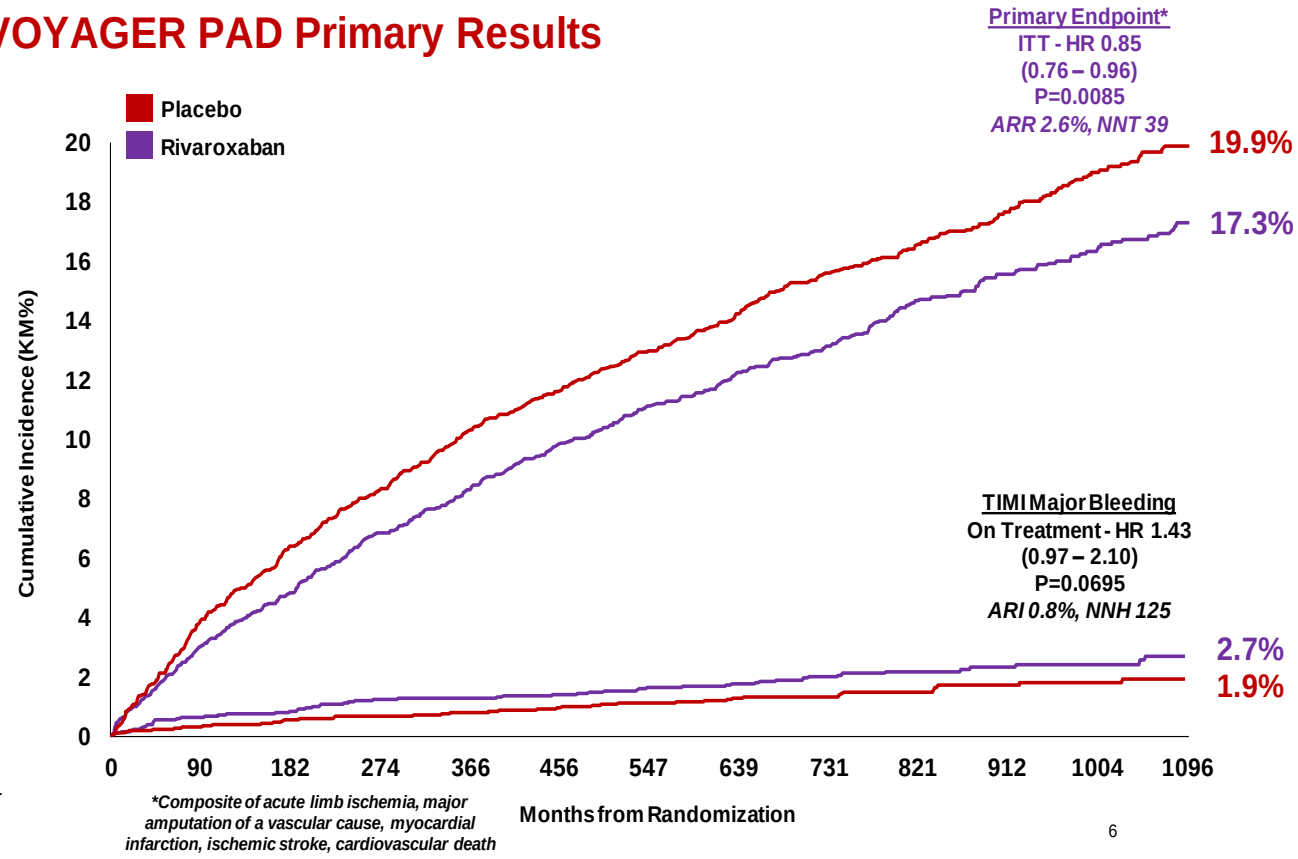
BACKGROUND

Risk of MACE and VOYAGER-PAD Main Results



Bonaca MP. Vasc Med. 2018 Dec;23(6):531-533.



Bonaca MP, et al. N Engl J Med. 2020 May 21;382(21):1994-2004.

AIM & METHODS

In PAD patients undergoing lower extremity revascularization (LER) for ischemic symptoms randomized to rivaroxaban 2.5 mg twice daily plus low dose aspirin versus aspirin alone:

- **To evaluate whether coronary artery disease (CAD) is associated with increased risk of major adverse cardiovascular events (MACE) compared to no CAD**
- **To evaluate whether the safety and efficacy of rivaroxaban after LER is consistent in patients with and without CAD particularly on MACE and subtype of Myocardial Infarction (MI)**

The presence of known CAD was reported by investigators at baseline and was defined as any known history including prior MI, coronary revascularization, other stable CAD. MI was defined according to the Universal Definition.

RESULTS

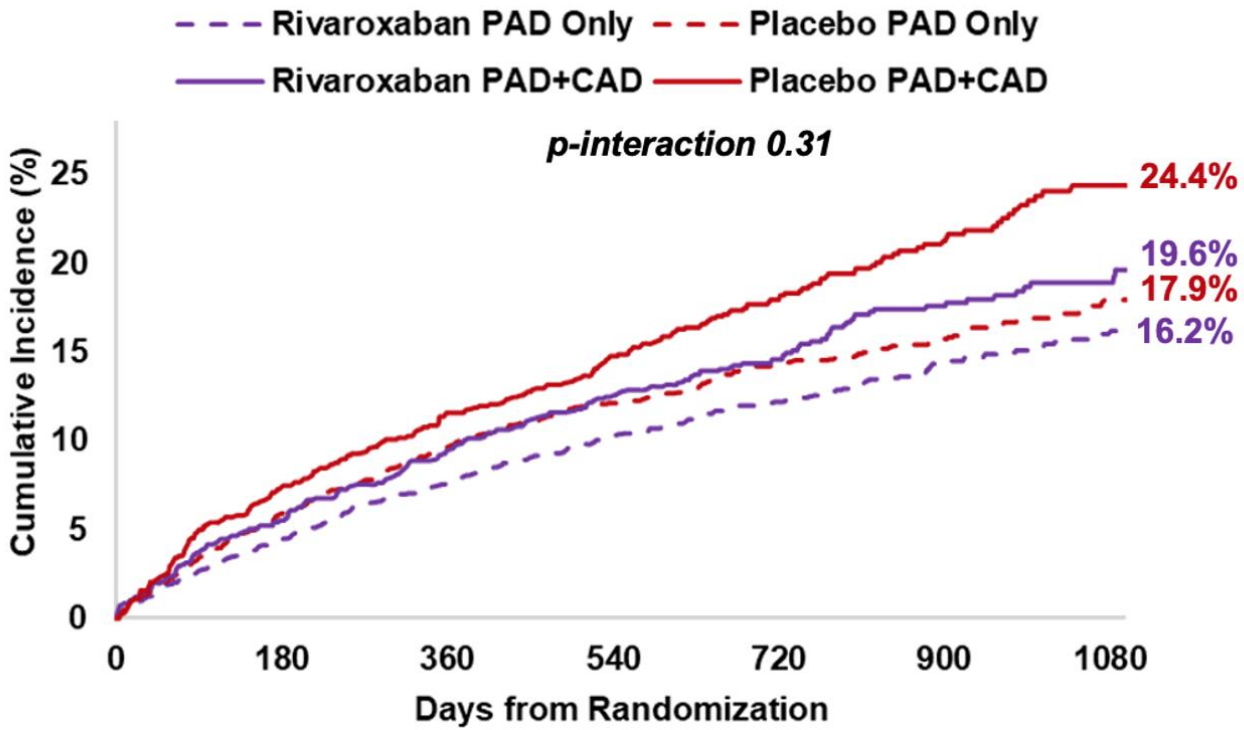
Baseline Characteristics

Baseline Characteristics	PAD+CAD N=2083	PAD Only N=4480	P-value
Median age (IQR) – yr	68 (62 – 74)	66 (60 – 72)	<0.0001
Female (%)	22	28	< 0.0001
White Caucasian (%)	79	82	0.0111
Hypertension (%)	90	77	<0.0001
Diabetes Mellitus (type 2) (%)	50	33	<0.0001
Hyperlipidemia (%)	73	54	<0.0001
Current smoking (%)	27	38	<0.0001
eGFR < 60 ml/min.1.73m^2 (%)	26	18	<0.0001
Prior MI (%)	34	0	<0.0001
Carotid stenosis ≥ 50% (%)	12	6	<0.0001
History of heart failure (%)	19	3	<0.0001

Baseline Characteristics	PAD+CAD N=2083	PAD Only N=4480	P-value
Qualifying revascularization			0.0155
Surgical (%)	31	34	
Endovascular (%)	69	66	
Reason for revascularization			0.0185
Claudication (%)	96	95	
Critical limb ischemia (%)	22	24	
PAD Characteristics			
Prior LER (%)	43	32	<0.0001
ABI (median, IQR)	0.58 (0.44 – 0.69)	0.54 (0.41 – 0.66)	<0.0001
Prior Major Amputation (%)	0.9	1.0	0.5920
Medications			
Statins (%)	90	76	<0.0001
ACE/ARB (%)	71	60	<0.0001
Clopidogrel at randomization (%)	54	49	<0.0001

RESULTS

Primary Efficacy Endpoint with and without CAD by Treatment



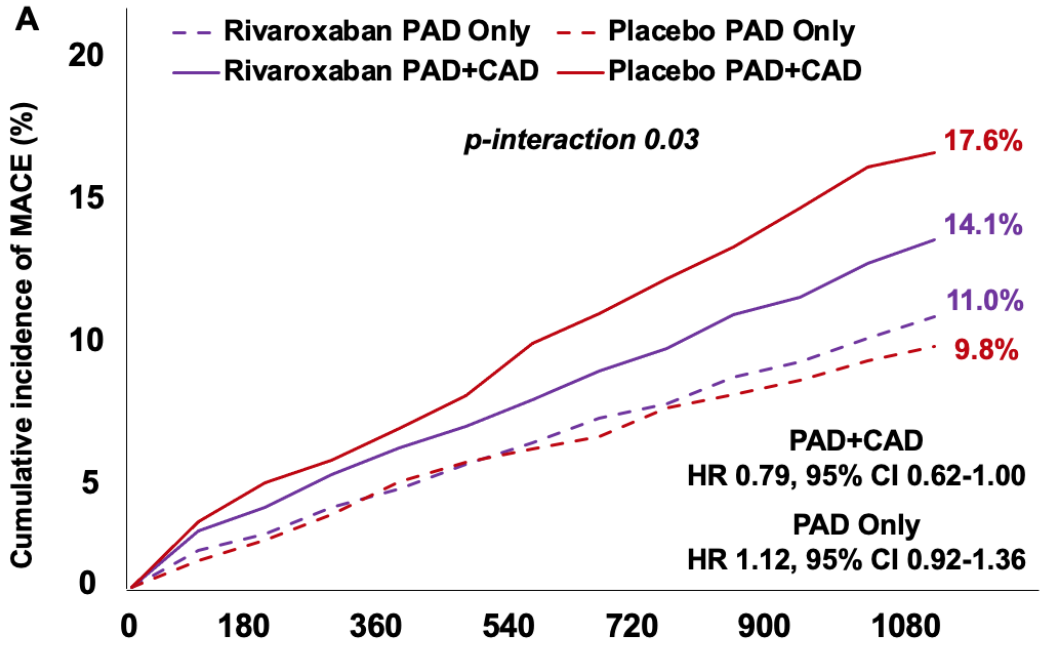
PAD+CAD
HR 0.79, 95% CI 0.65-0.96
ARR 4.8%, NNT 21

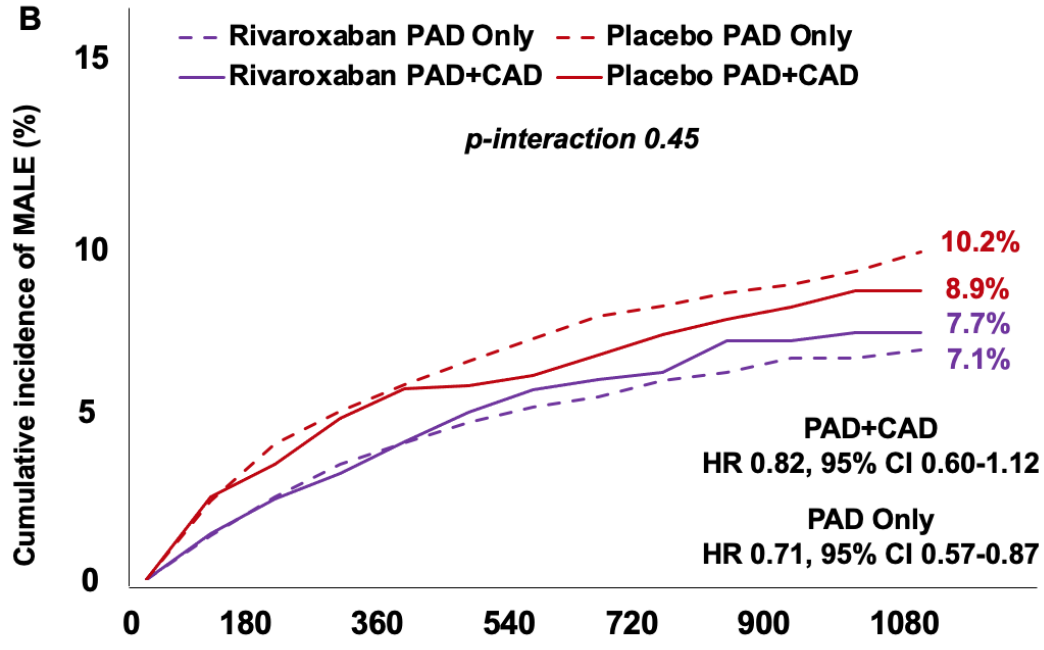
PAD Only
HR 0.89, 95% CI 0.77-1.03
ARR 1.7%, NNT 59

No. at Risk PAD Only							
Placebo	2257	2096	1997	1929	1561	997	481
Rivaroxaban	2223	2098	2004	1935	1568	1014	503
No. at Risk PAD + CAD							
Placebo	1021	936	887	848	646	411	202
Rivaroxaban	1062	985	937	902	709	455	229

RESULTS

MACE (A) and MALE (B) with and without CAD by Treatment



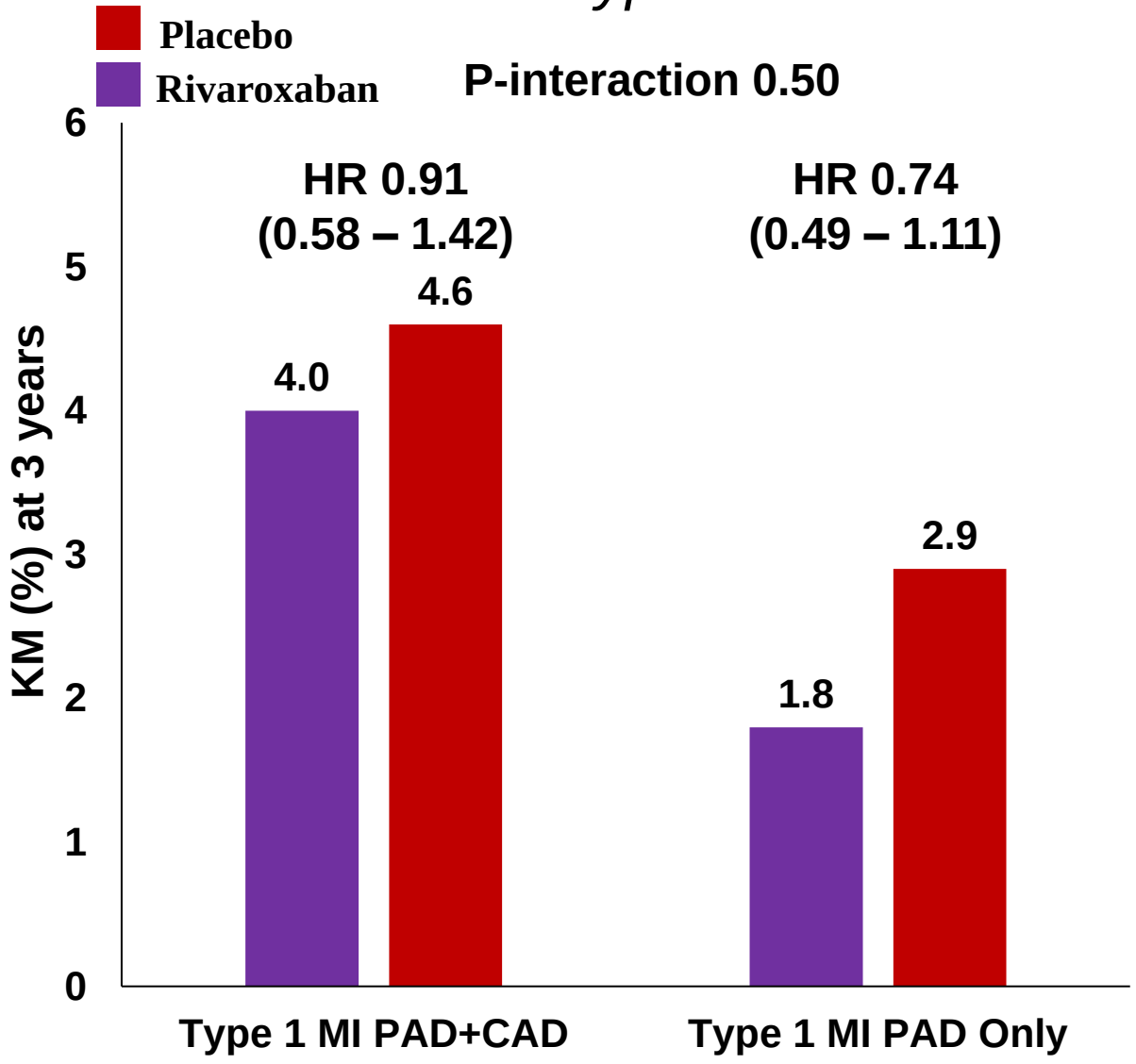


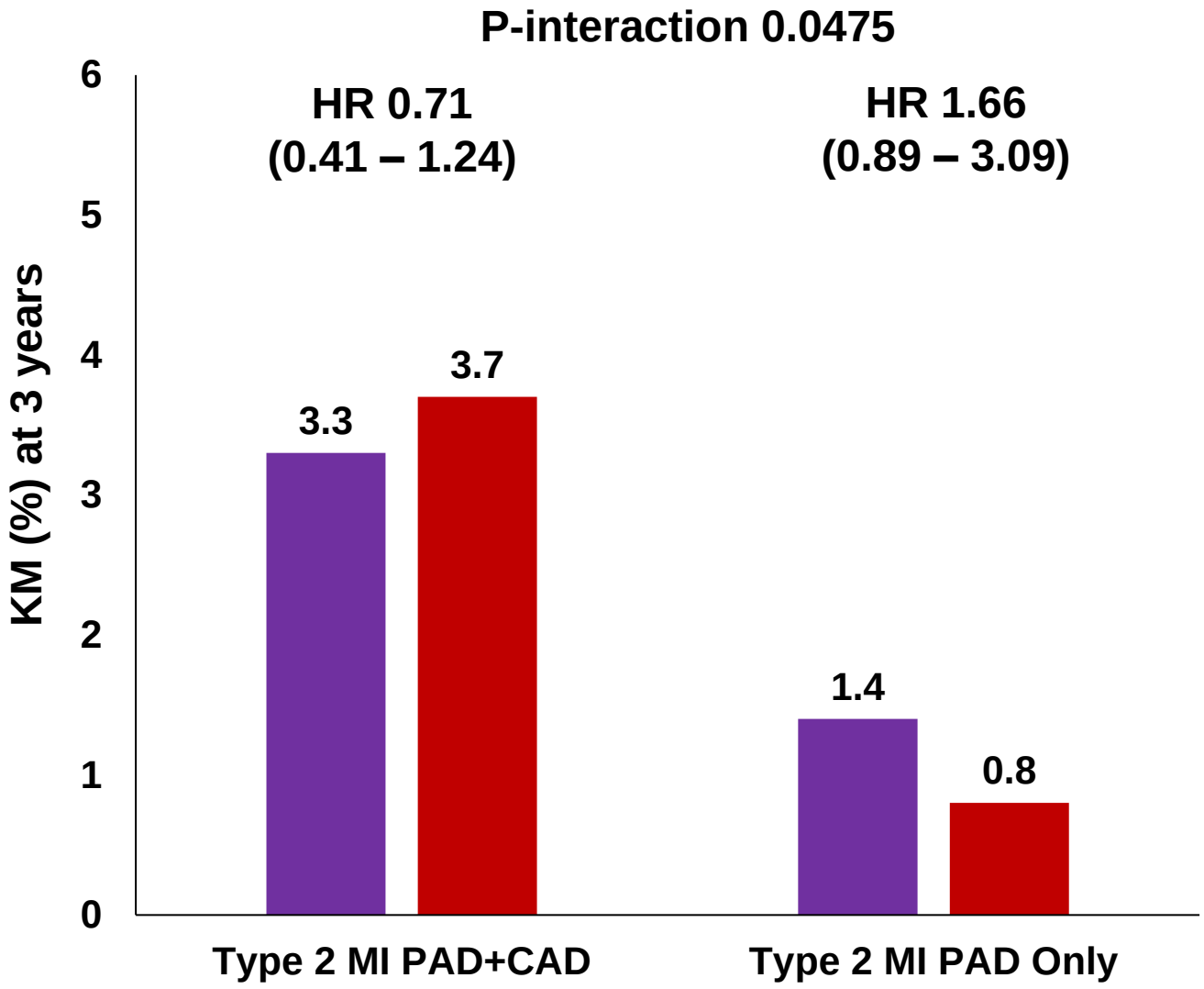
No. at Risk PAD Only							
Placebo	2257	2183	2112	2068	1652	1060	513
Rivaroxaban	2223	2146	2080	2026	1614	1022	498
No. at Risk PAD+CAD							
Placebo	1021	966	934	892	671	420	207
Rivaroxaban	1062	1007	976	953	731	465	229

No. at Risk PAD Only							
Placebo	2257	2109	2028	1971	1567	982	464
Rivaroxaban	2223	2112	2026	1971	1563	990	482
No. at Risk PAD+CAD							
Placebo	1021	957	918	892	666	424	205
Rivaroxaban	1062	995	960	935	715	456	227

RESULTS

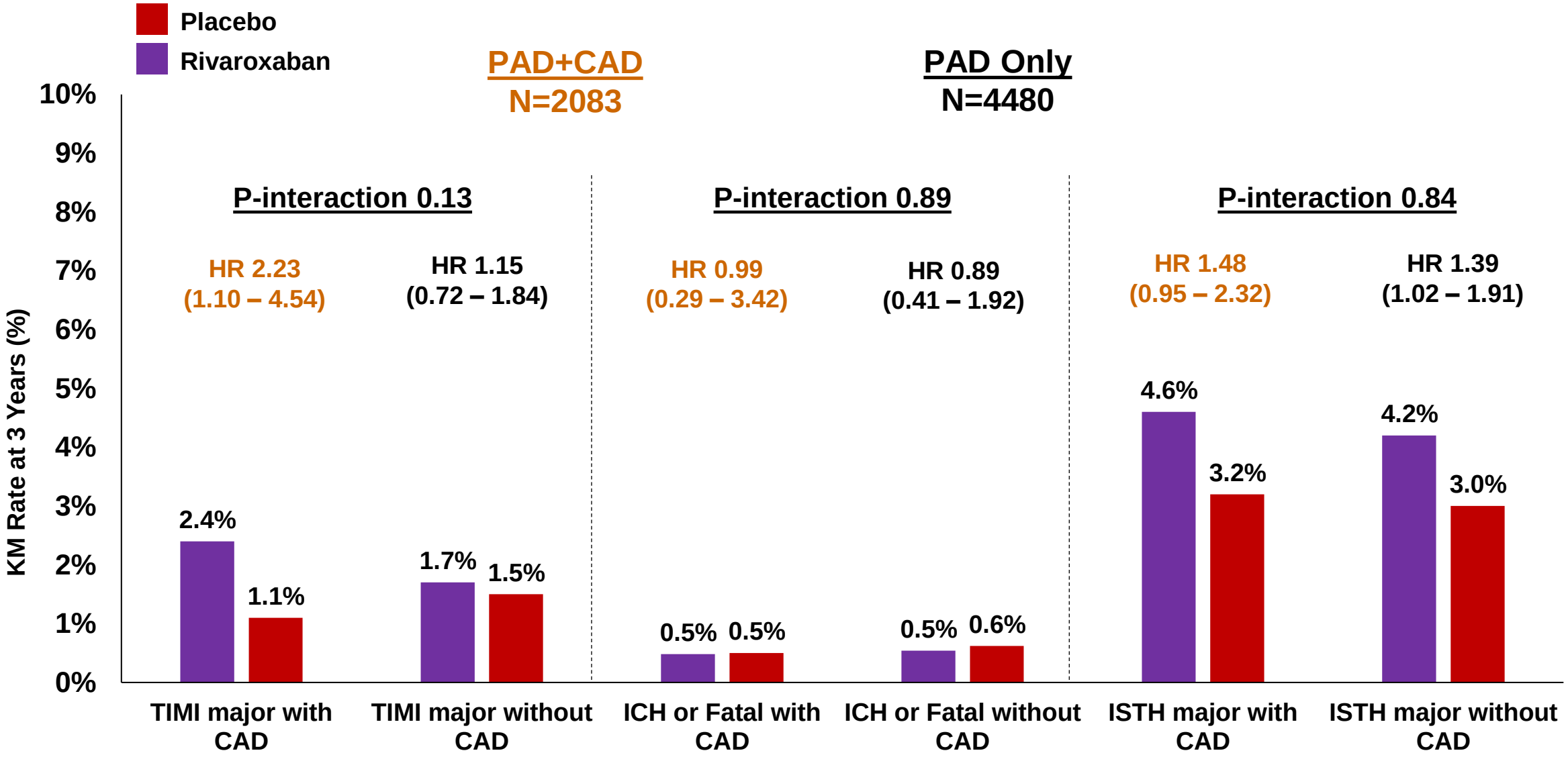
Type of MI with and without CAD by Treatment





RESULTS

Safety of Rivaroxaban vs Placebo With and Without CAD



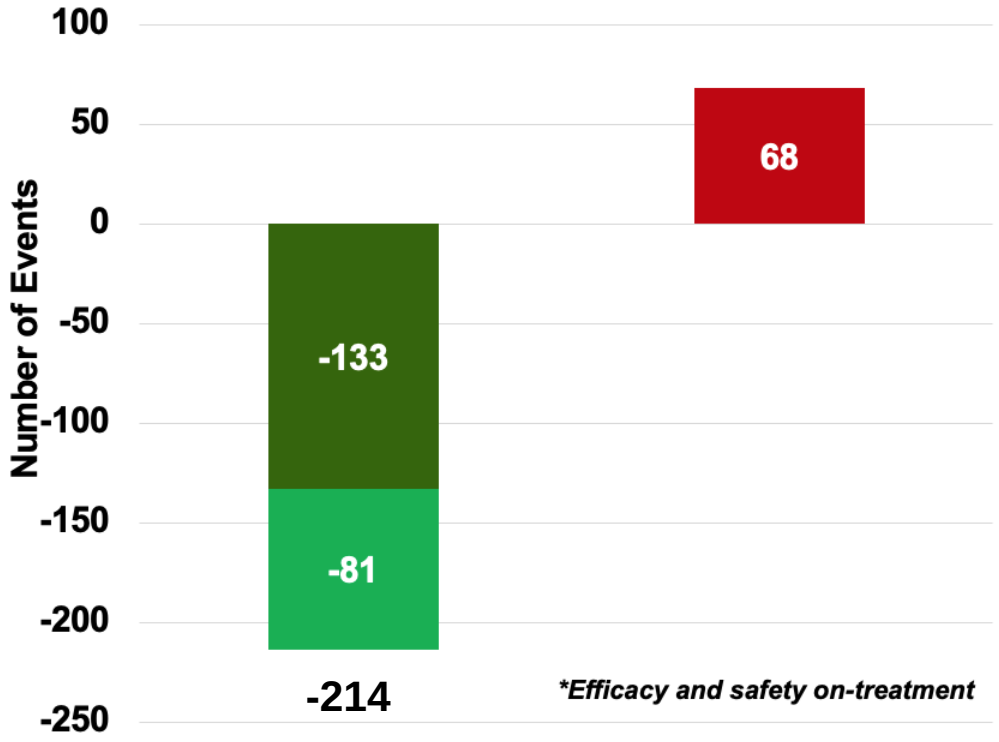
RISK / BENEFIT: ON TREATMENT

First Events Prevented / Caused for 10,000 Patients Treated* for 1 Year

PAD+CAD

Ischemic Events Prevented
MACE
HR 0.76 (95% CI 0.57-1.01)
MALE
HR 0.76 (95% CI 0.52-1.10)

Principal Safety Outcome Events Caused
HR 2.23
(95% CI 1.10-4.54)
(TIMI major bleeding)

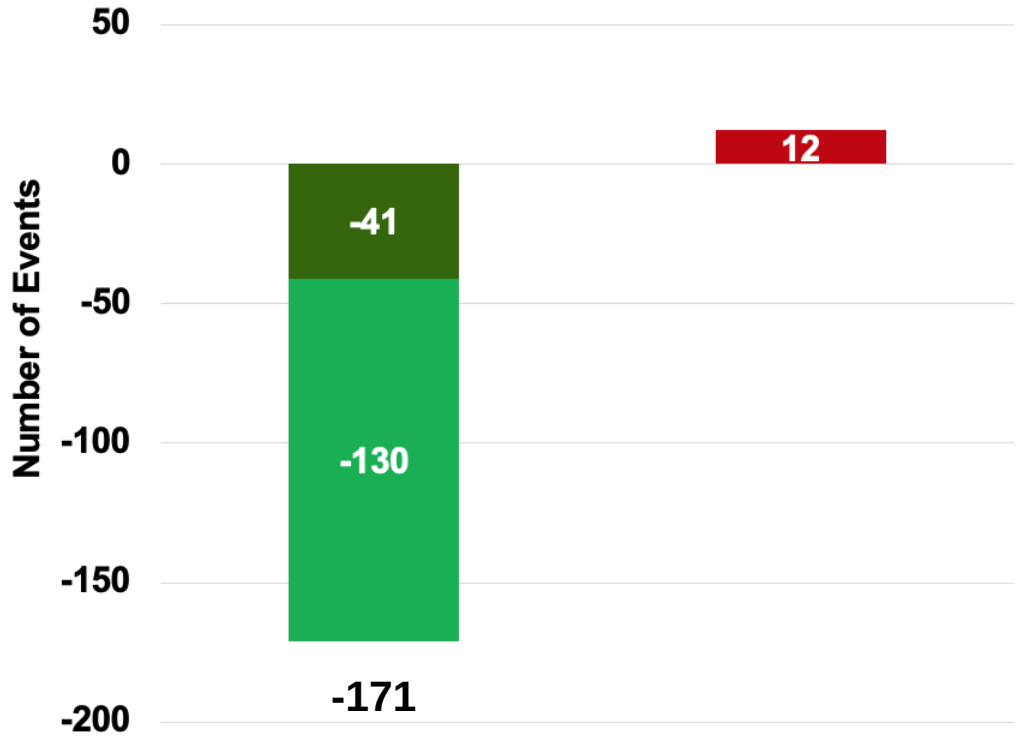


*Efficacy and safety on-treatment

PAD Only

Ischemic Events Prevented
MACE
HR 0.86 (95% CI 0.67-1.10)
MALE
HR 0.65 (95% CI 0.51-0.83)

Principal Safety Outcome Events Caused
HR 1.15
(95% CI 0.72-1.84)
(TIMI major bleeding)



SUMMARY & CONCLUSION

In patients with lower extremity PAD undergoing revascularization for ischemia:

- **Patients with PAD and CAD appear to have higher rates of MACE relative to those with PAD and no CAD.**
- **The efficacy and safety of rivaroxaban in PAD are consistent regardless of CAD with no significant interactions, however, the absolute benefits of rivaroxaban appear greater in those with CAD particularly for MACE including MI.**
- **Although exploratory and hypothesis generating, heterogeneity in the benefit of rivaroxaban by MI subtype may be an avenue of investigation in understanding the differing results of antithrombotic therapies for MACE reduction in populations selected on the basis of CAD versus PAD.**

An Affiliate of:

THANK YOU

American Heart Association.

Scientific Sessions

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