Rivaroxaban plus aspirin versus with aspirin in patients with prior percutaneous coronary Intervention (PCI): Insights from the COMPASS Trial

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COMPASS PCI

Background

- The COMPASS trial demonstrated dual pathway inhibition (DPI) with rivaroxaban 2.5 mg twice-daily plus aspirin 100 mg once-daily versus aspirin 100 mg once-daily reduced the primary MACE outcome of cardiovascular death, MI, or stroke as well as mortality in patients with chronic coronary syndromes or peripheral artery disease.
- Patients undergoing PCI are routinely treated with DAPT
- However, the efficacy of DPI with prior PCI is less well studied

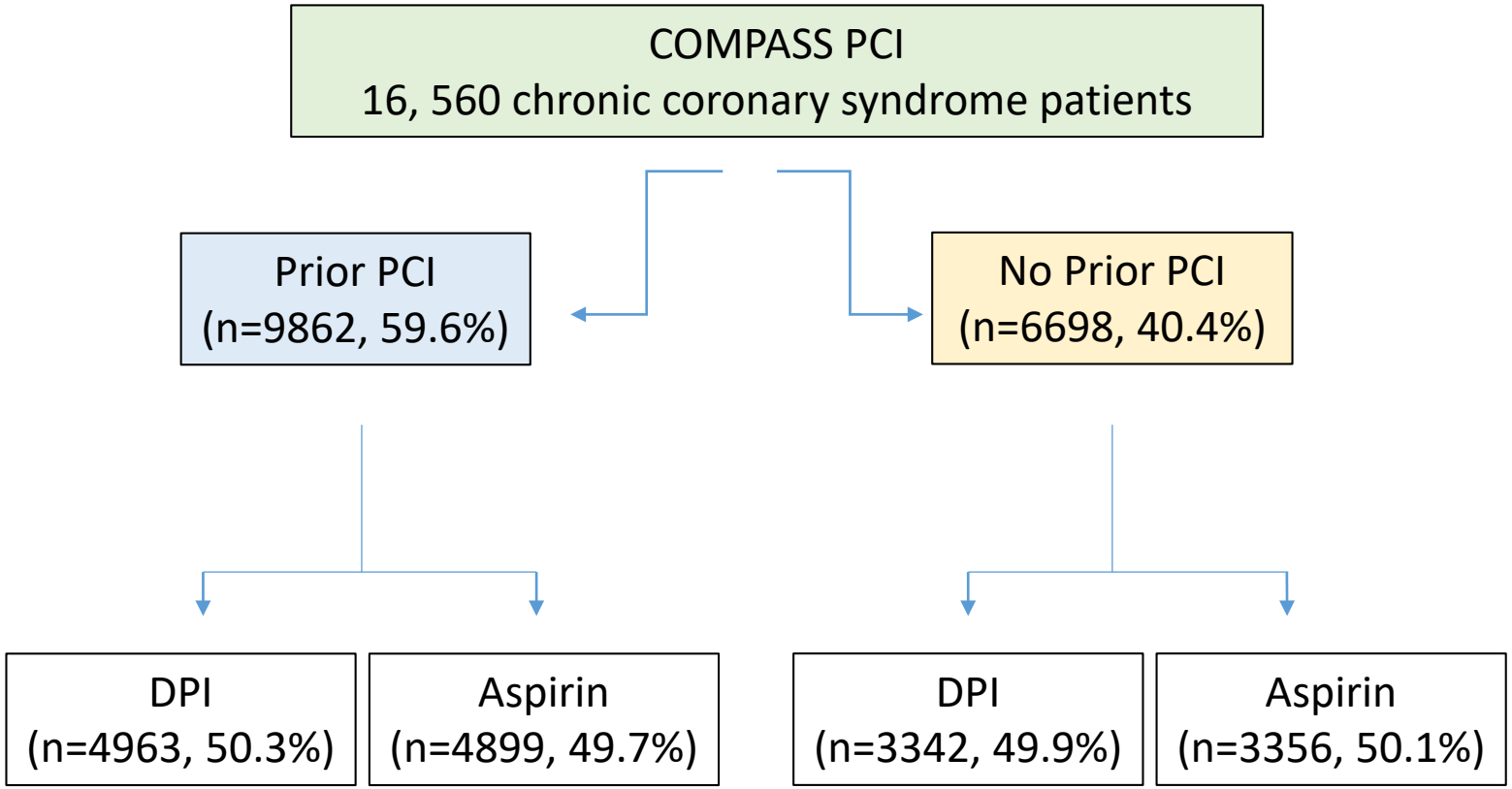
DAPT=dual antiplatelet therapy; MACE=major adverse cardiac event; MI=myocardial infarction; PCI=percutaneous coronary intervention

Objectives

- In a pre-specified sub-group analysis from COMPASS, we examined the impact of dual pathway inhibition compared to aspirin alone in chronic coronary syndrome patients with or without prior PCI.
- Among patients with a prior PCI, we studied the effects of treatment according to the timing of prior PCI.

PCI=percutaneous coronary intervention

Study Flow


COMPASS PCI
16, 560 chronic coronary syndrome patients
Prior PCI
(n=9862, 59.6%)
No Prior PCI
(n=6698, 40.4%)
DPI
(n=4963, 50.3%)
Aspirin
(n=4899, 49.7%)
DPI
(n=3342, 49.9%)
Aspirin
(n=3356, 50.1%)

Baseline Characteristics

COMPASS PCI

	Prior PCI (n=9862)	No Prior PCI (n=6698)
Age, years	68·2 (7·8)	68·5 (7·9)
Female sex	1918 (19·4%)	1461 (21·8%)
Risk factors		
Cholesterol, mmol/L	4·1 (1·0)	4·2 (1·1)
Tobacco use	2082 (21·1%)	1281 (19·1%)
Hypertension	7352 (74·5%)	5133 (76·6%)
Peripheral arterial disease	1731 (17·6%)	1563 (23·3%)
Diabetes	3516 (35·7%)	2558 (38·2%)
Previous MI	7372 (74·8%)	3993 (59·6%)
Previous stroke	267 (2·7%)	280 (4·2%)
Medication		
ACE inhibitor or ARB	7266 (73·7%)	4636 (69·2%)
Beta-blocker	7304 (74·1%)	4964 (74·1%)
Lipid-lowering agent	9250 (93·8%)	5977 (89·2%)

Data are mean (SD) or n (%). eGFR=estimated glomerular filtration rate. MI=myocardial infarction. ACE inhibitor=angiotensin-converting enzyme inhibitor. ARB=angiotensin receptor blocker

Prior PCI characteristics according to treatment received

COMPASS PCI

PCI Occurrence	Low-dose rivaroxaban plus aspirin (n=4963)	Aspirin alone (n=4899)
Timing of prior PCI		
Less than one year prior to randomization	249 (5·0%)	231 (4·7%)
1 year to <2 years prior to randomization	1008 (20·3%)	897 (18·3%)
2 years to <3 years prior to randomization	616 (12·4%)	663 (13·5%)
3 years or more prior to randomization	3089 (62·2%)	3105 (63·4%)
PCI type		
Single-vessel PCI	3016 (60·8%)	3071 (62·7%)
Multi-vessel PCI	1947 (39·2%)	1828 (37·3%)

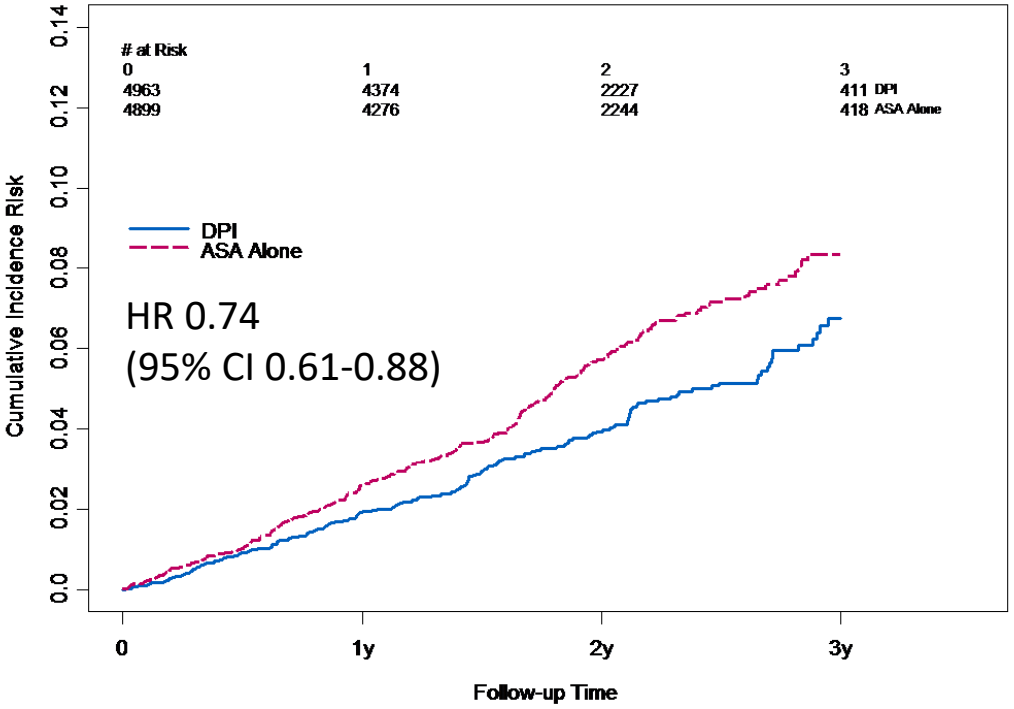
Data are n (%). PCI=percutaneous coronary intervention.

Primary Efficacy Endpoint
CV death, MI or stroke (ITT)

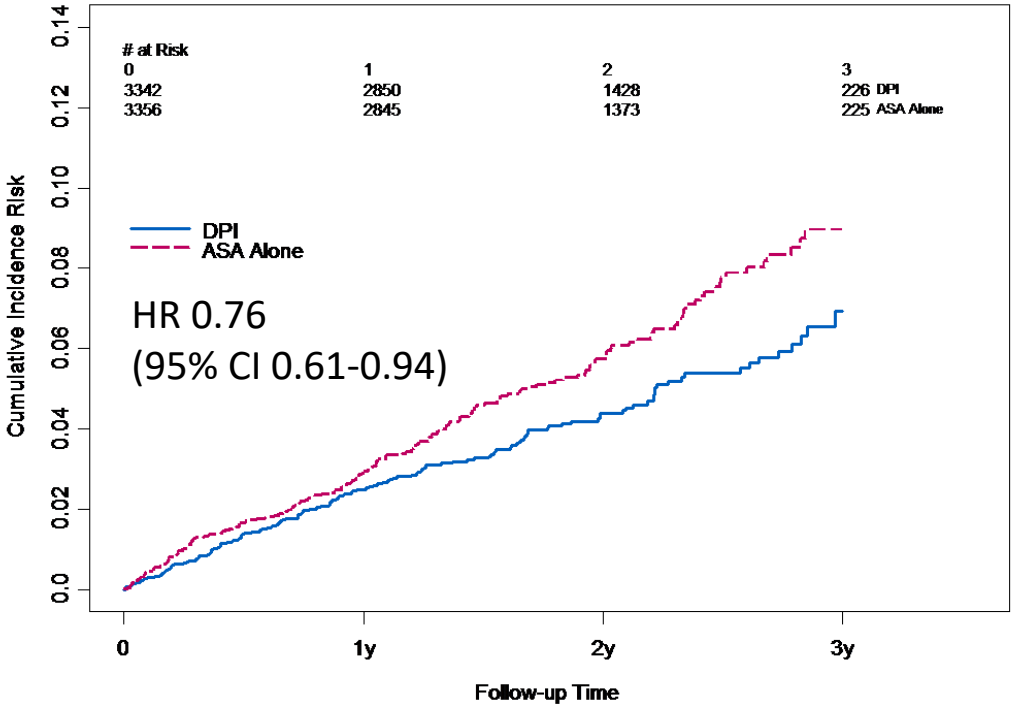
COMPASS PCI

Interaction p=0.85

Prior PCI



No Prior PCI

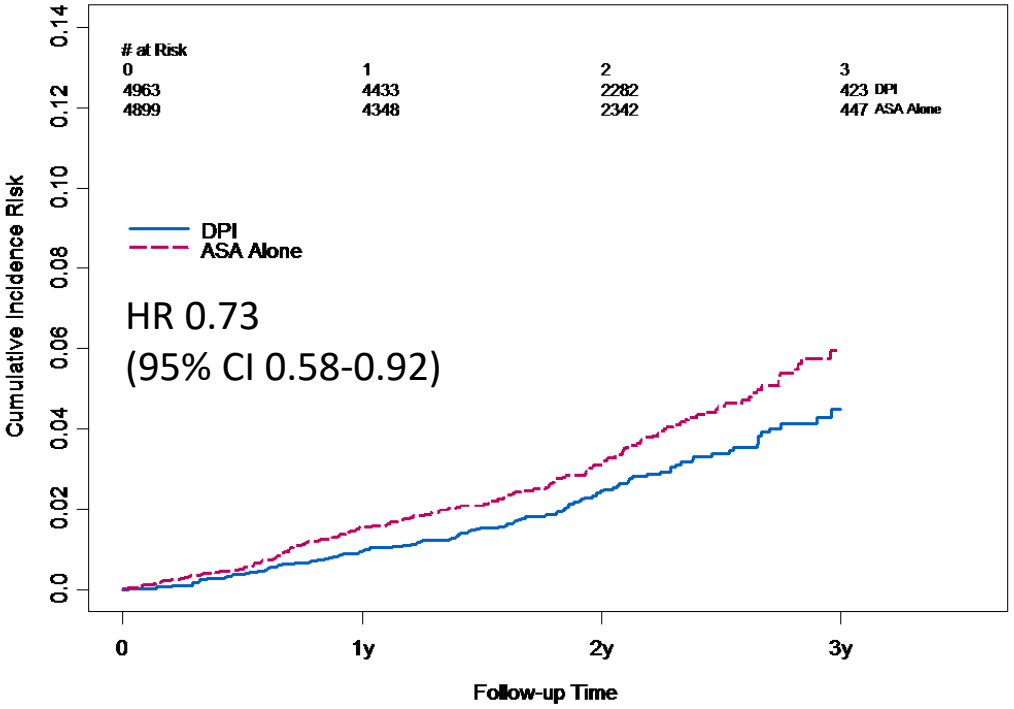


Secondary Efficacy Endpoint
All-Cause Death (ITT)

COMPASS PCI

Interaction p=0.59

Prior PCI



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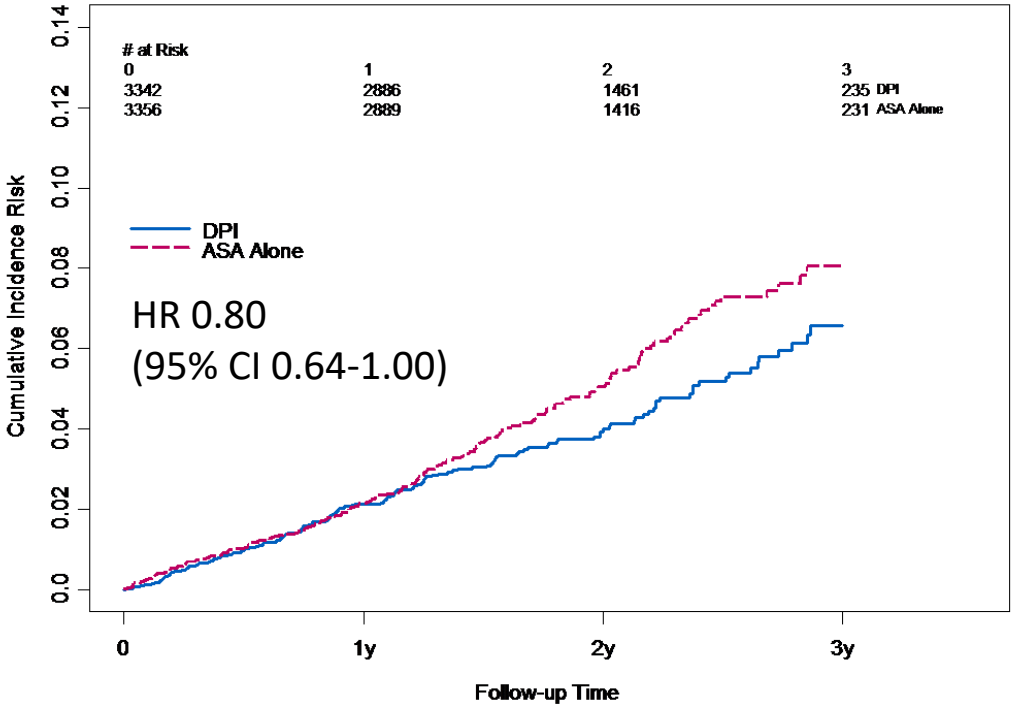

Safety Endpoint
Major Bleeding*

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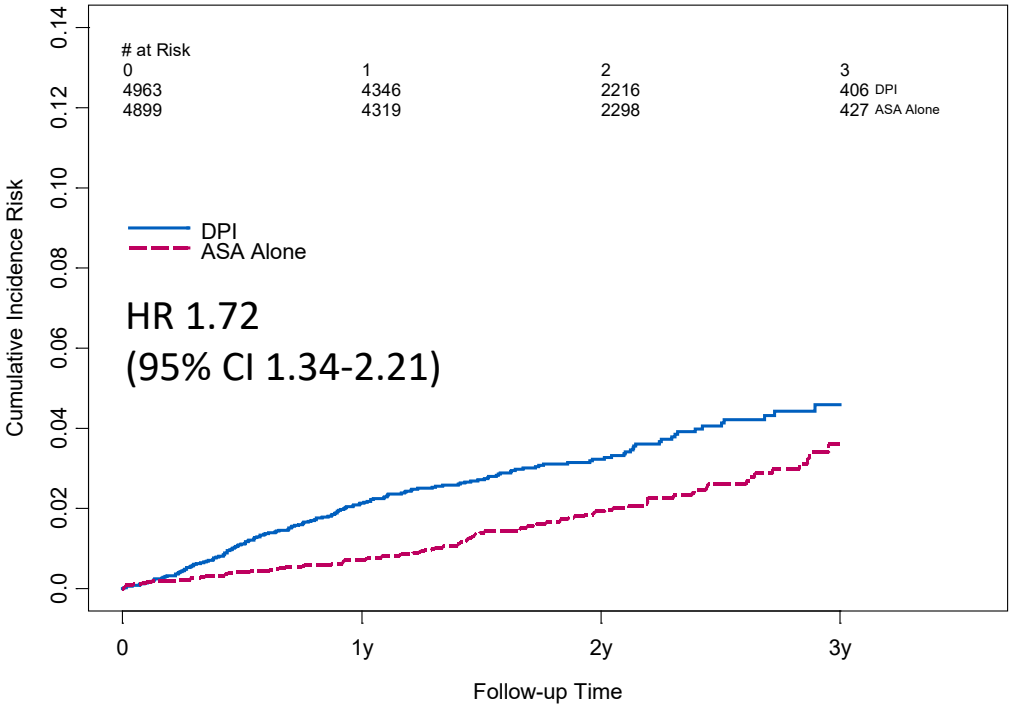
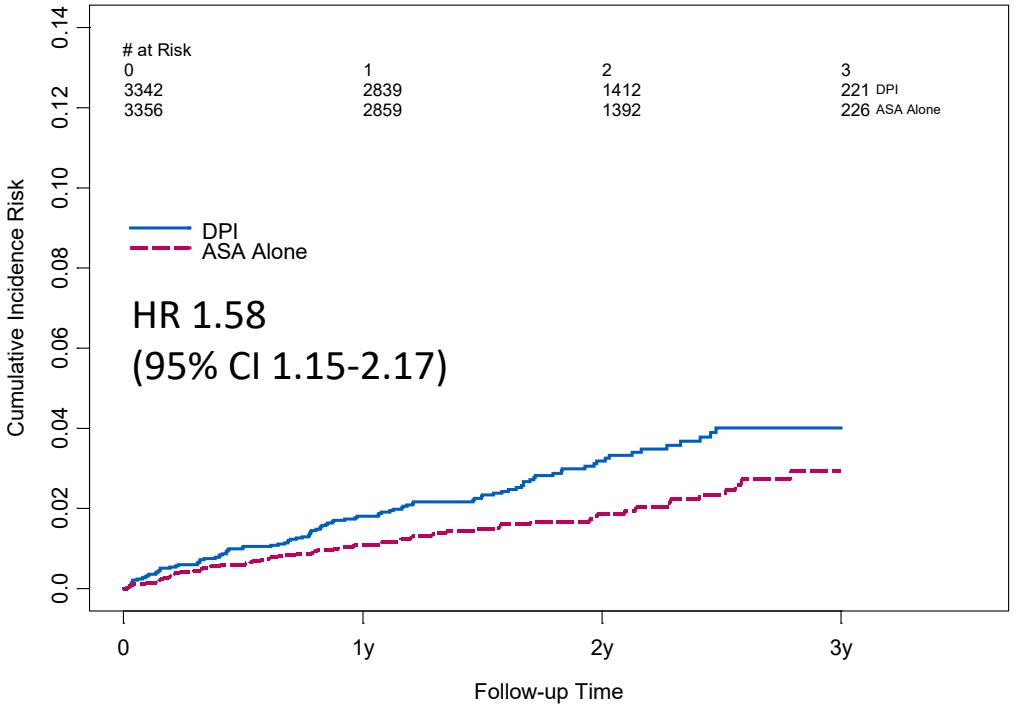
Interaction p=0.68

Prior PCI



No Prior PCI



*The primary safety outcome was modified International Society of Thrombosis and Hemostasis (ISTH) major bleeding, defined as: i) fatal bleeding and/or ii) symptomatic bleeding in a critical area or organ or bleeding into the surgical site requiring re-operation and/or iii) bleeding leading to hospitalization (including presentation to an acute care facility without an overnight stay). Symptomatic bleeding into a critical organ or area included intracranial, intraspinal, intraocular, retroperitoneal, intraarticular or pericardial, or intramuscular with compartment syndrome.

Other Bleeding Endpoints

		Low-dose rivaroxaban plus aspirin (n=8305)		Aspirin alone (n=8255)		Low-dose rivaroxaban plus aspirin vs· aspirin alone	
Event	Subgroup	Subgroup n	Patients with events (%)	Subgroup n	Patients with events (%)	HR (95% CI)	P value for interaction
Major Bleed	Prior PCI	4963	165 (3·3%)	4899	96 (2·0%)	1·72 (1·34-2·21)	**0·68**
Major Bleed	No prior PCI	3342	98 (2·9%)	3356	62 (1·8%)	1·58 (1·15-2·17)	·
Minor Bleed	Prior PCI	4963	489 (9·9%)	4899	291 (5·9%)	1·71 (1·48-1·98)	**0·74**
Minor Bleed	No prior PCI	3342	284 (8·5%)	3356	162 (4·8%)	1·78 (1·47-2·16)	·
Fatal Bleed	Prior PCI	4963	7 (0·1%)	4899	2 (<0.1%)	3·47 (0·72-16·7)	**0·15**
Fatal Bleed	No prior PCI	3342	7 (0·2%)	3356	8 (0·2%)	0·87 (0·32-2·41)	·
ICH Bleed	Prior PCI	4963	17 (0·3%)	4899	13 (0·3%)	1·30 (0·63-2·68)	**0·52**
ICH Bleed	No prior PCI	3342	9 (0·3%)	3356	10 (0·3%)	0·89 (0·36-2·20)	·

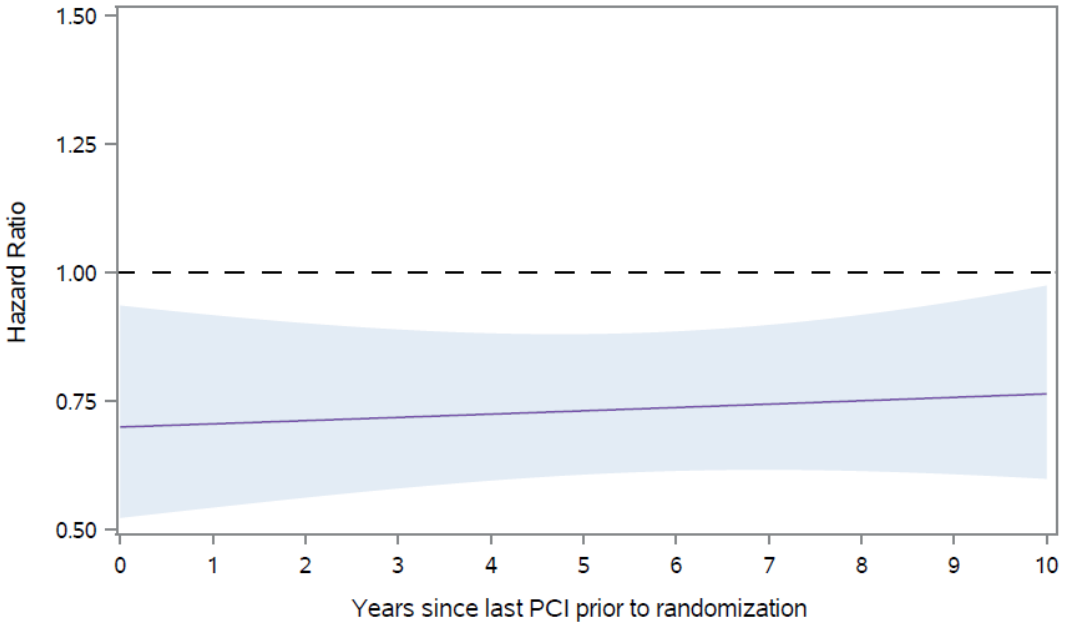
Data are n (%) or HR (95% CI). HR=hazard ratio. PCI=percutaneous coronary intervention. ICH=intracranial hemorrhage

Benefit of DPI vs Aspirin

as a function of time from the most recent percutaneous coronary intervention

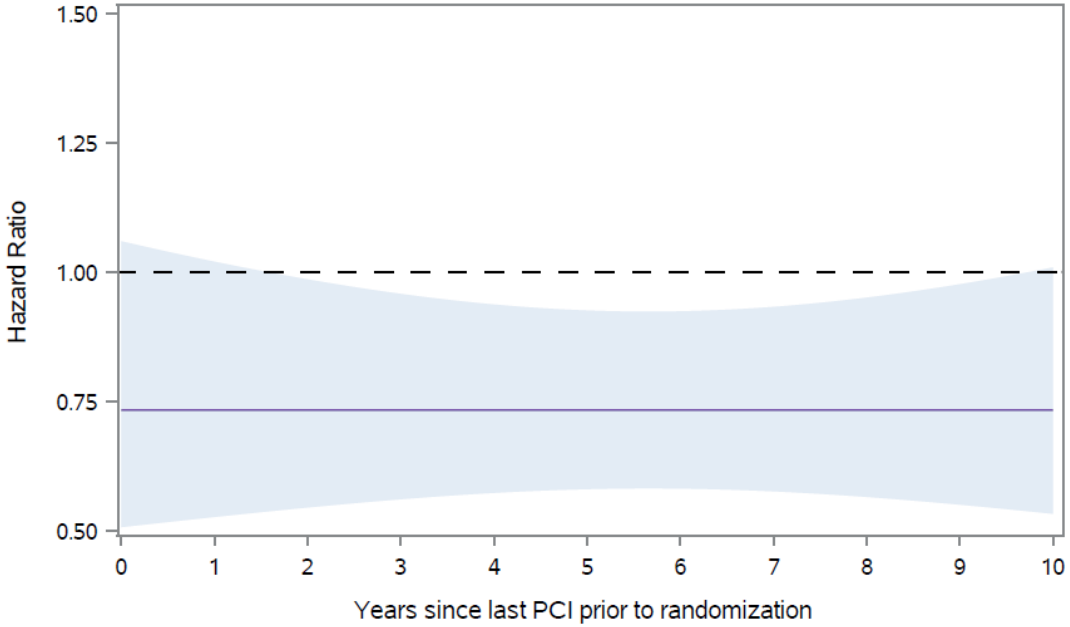
COMPASS PCI

CV Death, MI, Stroke



The p-value of interaction between treatment group and time since percutaneous coronary intervention was 0.66

All-cause mortality



The p-value of interaction between treatment group and time since percutaneous coronary intervention was greater than 0.99

Conclusions

- DPI compared with aspirin alone:
  - Produced consistent reductions in CV death, MI, stroke as well as all-cause death with or without prior PCI
  - Increased major bleeding without a significant increase in fatal bleeding or intracranial hemorrhage
- In patients with prior PCI:
  - Consistent reductions in CV death, MI, stroke as well as all-cause death were demonstrated with DPI irrespective of the timing of prior PCI (as far back as 10-years)