Efficacy and Safety of Rivaroxaban in Patients with PAD with Concomitant Diabetes After Lower Extremity Revascularization

Cecilia C Low Wang, E. Sebastian Debus, Mark Nehler, Manesh Patel, Sonia Anand, Matthew Jackson, Michael Szarek, Connie Hess, Warren Capell, Eva Muehlhofer, Lloyd Haskell, Scott D Berkowitz, Rupert Bauersachs, Marc P Bonaca, on behalf of the VOYAGER PAD investigators

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Disclosures

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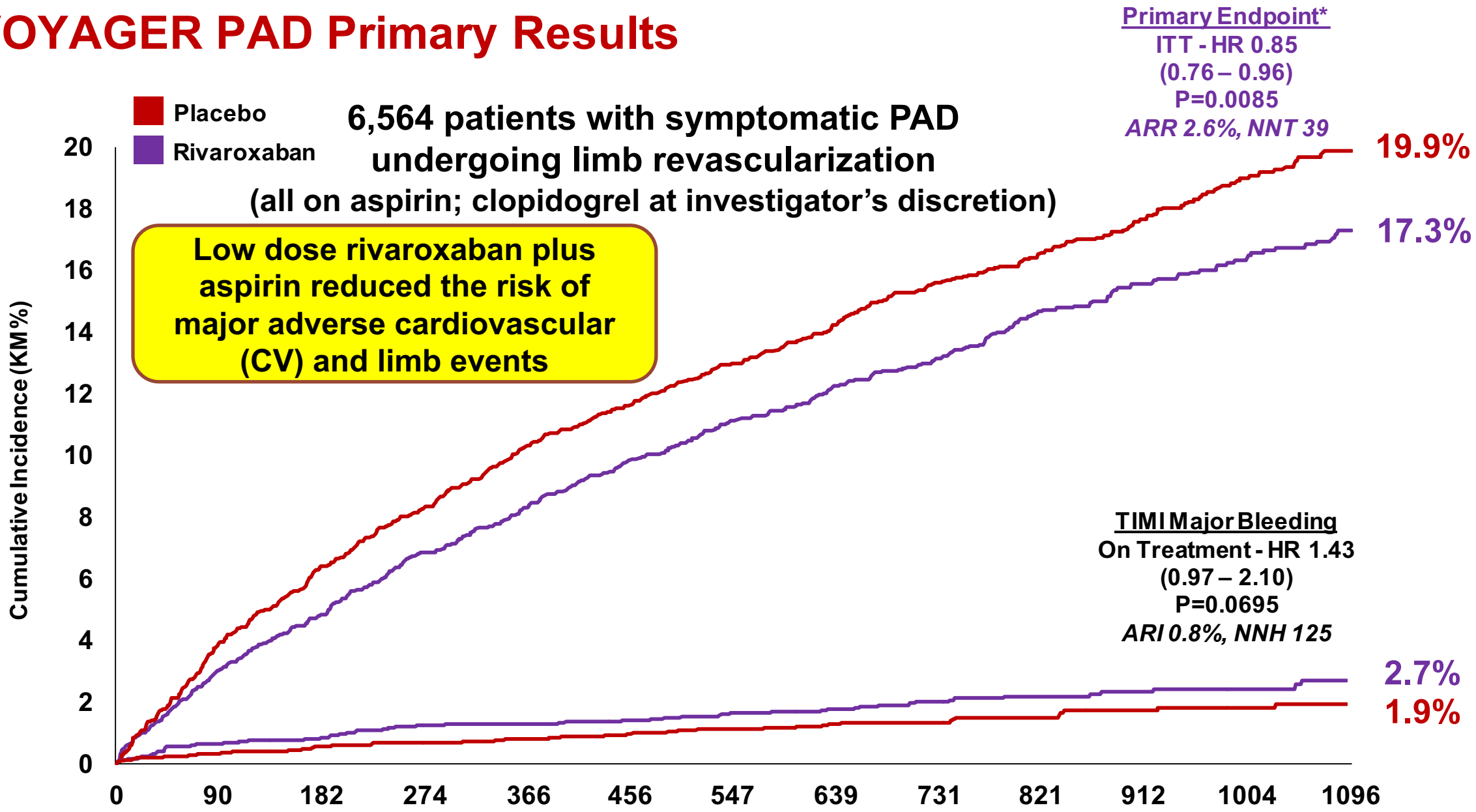
VOYAGER PAD Primary Results



*Composite of acute limb ischemia, major amputation of a vascular cause, myocardial infarction, ischemic stroke, cardiovascular death

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Bonaca MP…Hiatt WR. NEJM 2020

Aims

- To characterize the risk profile of patients with symptomatic PAD after LER based on diabetes status at baseline

- To assess the consistency of efficacy and safety of rivaroxaban for vascular events and bleeding on the basis of diabetes at baseline

Methods

- Prespecified analysis by DM identified at baseline

- Primary efficacy endpoint composite of acute limb ischemia, major amputation of vascular etiology, MI, ischemic stroke, CV death

- Principal safety outcome TIMI major bleeding

- All efficacy and safety outcomes adjudicated by blinded CEC

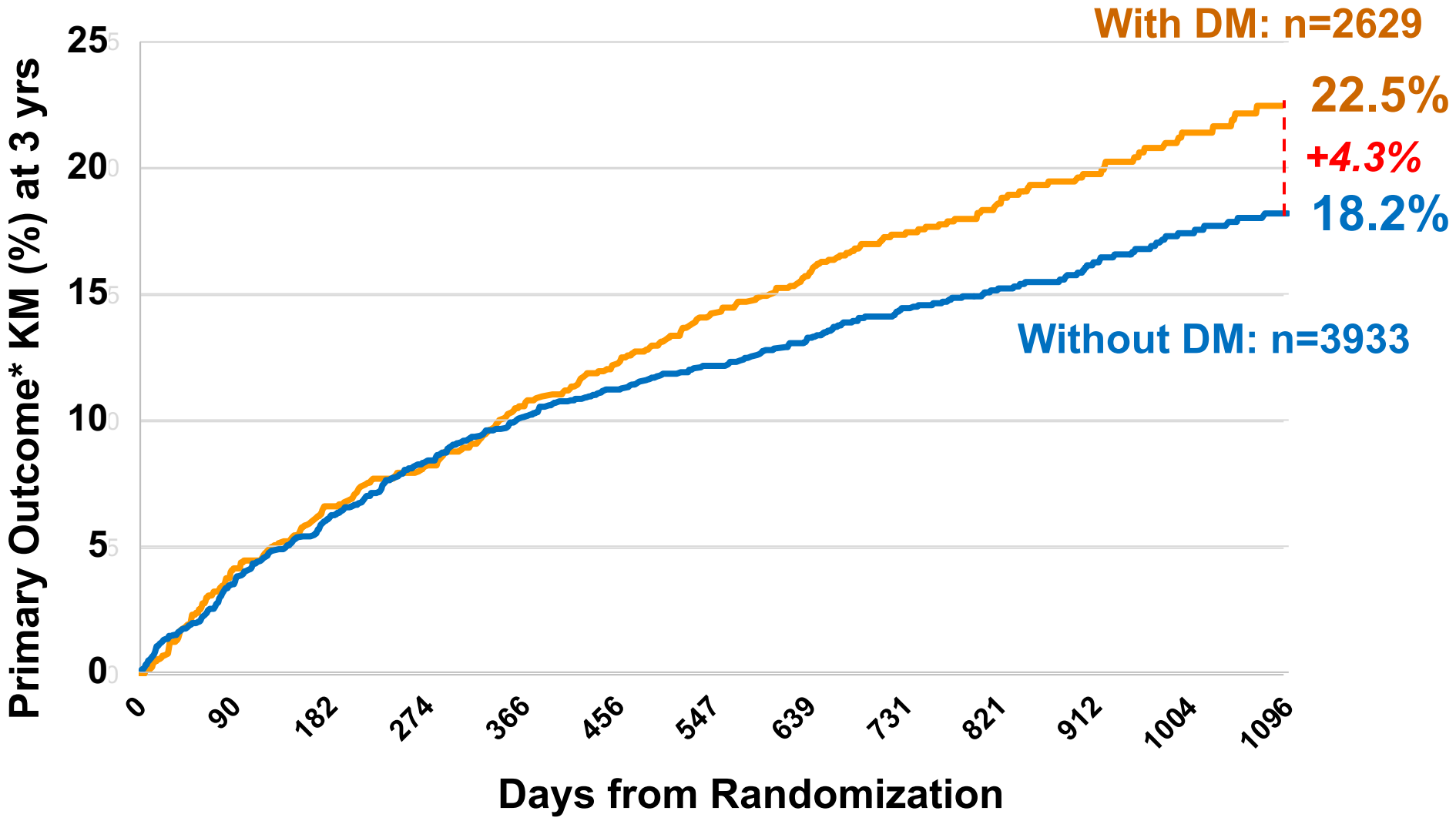
- Exploratory analysis of risk for bleeding events (high vs low)

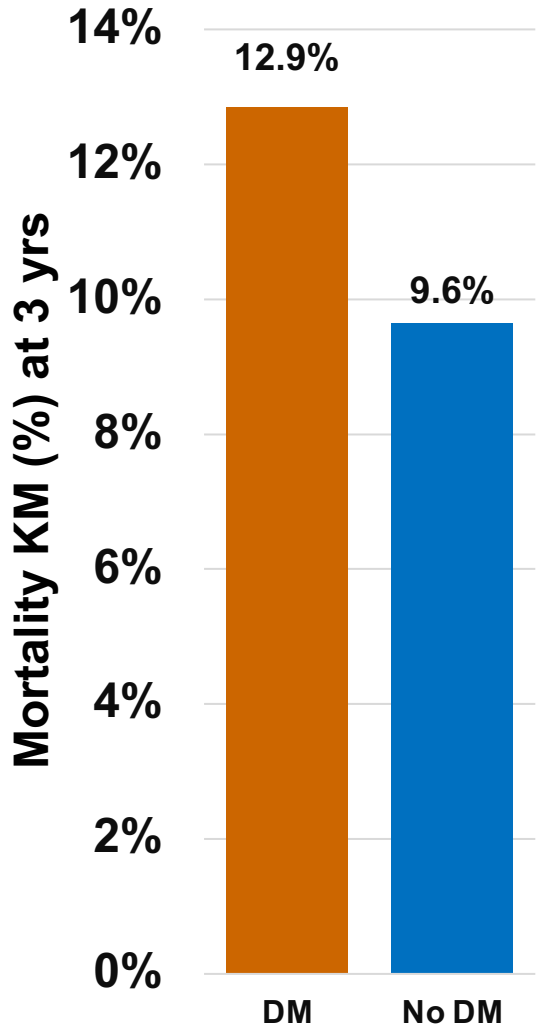
- On treatment exploratory analysis, i.e. occurrence of first outcome event within 2 days of last dose of study drug

Baseline Characteristics (n=6564)

	DM (40%; n=2629) T2DM: 96%, T1DM: 4%	No DM (60%; n=3933)	p-value
Age (yr), median	67	66	<0.0001
Female (%)	27	25	0.1077
Caucasian (%)	76	84	<0.0001
BMI (kg/m^2), median	27	25	<0.0001
Current smoking (%)	28	39	<0.0001
HTN (%)	89	77	<0.0001
eGFR < 60 ml/min/1.73m^2 (%)	27	16	<0.0001
Coronary Artery Disease (%)	40	26	<0.0001
Statin (%)	83	78	<0.0001
ACEi or ARB (%)	73	57	<0.0001
Clopidogrel use at randomization (%)	56	47	<0.0001
Ankle Brachial Index, Median (IQR)	0.54 (0.28 – 0.80)	0.53 (0.28 – 0.78)	0.0122
History of Amputation (%)	10 (80% below ankle)	3	<0.0001
Baseline CLI (%)	27	21	<0.0001
Surgical revascularization: Surgical (%)	25	38	<0.0001

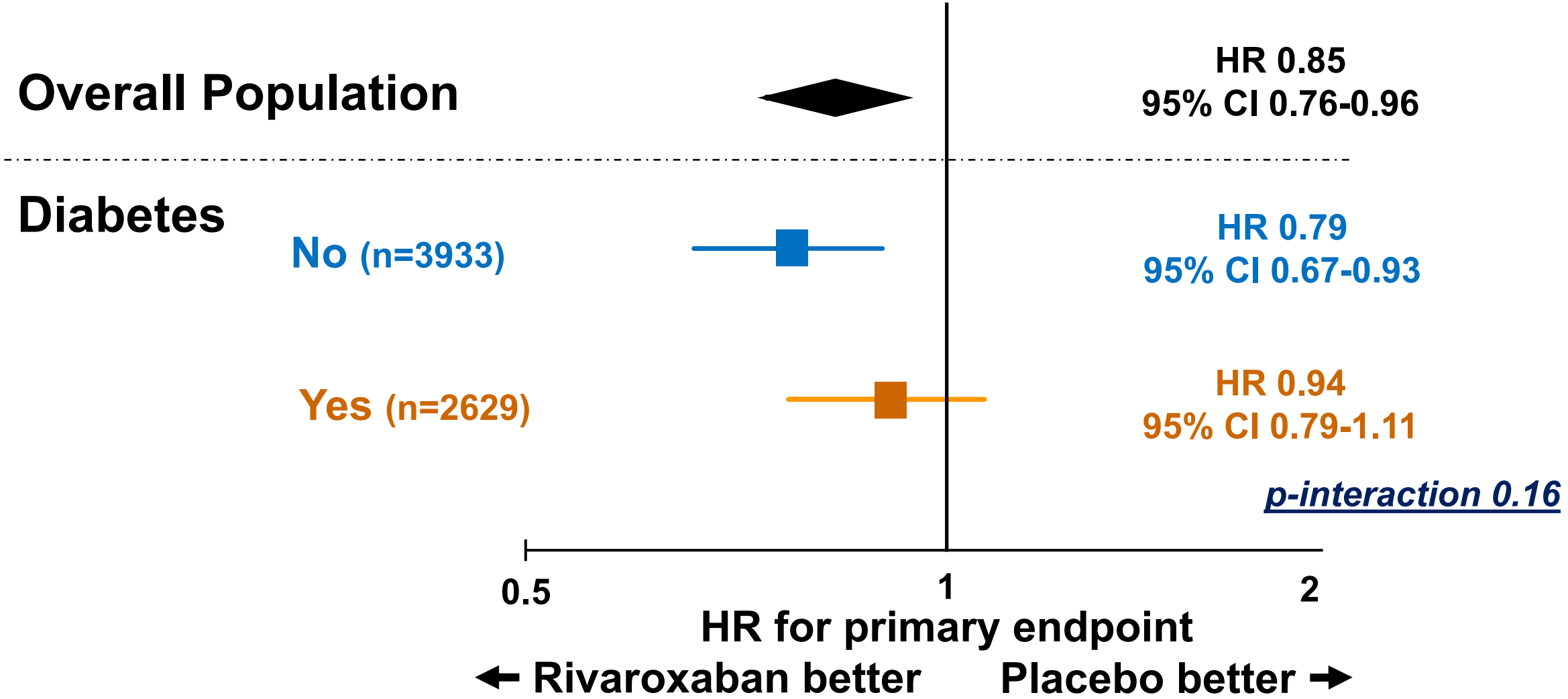
Three Year Outcomes in those With and Without Diabetes Randomized to Placebo





*ALI, major amputation of a vascular cause, MI, ischemic stroke, CV death

Primary Endpoint* in Patients With and Without Diabetes Mellitus



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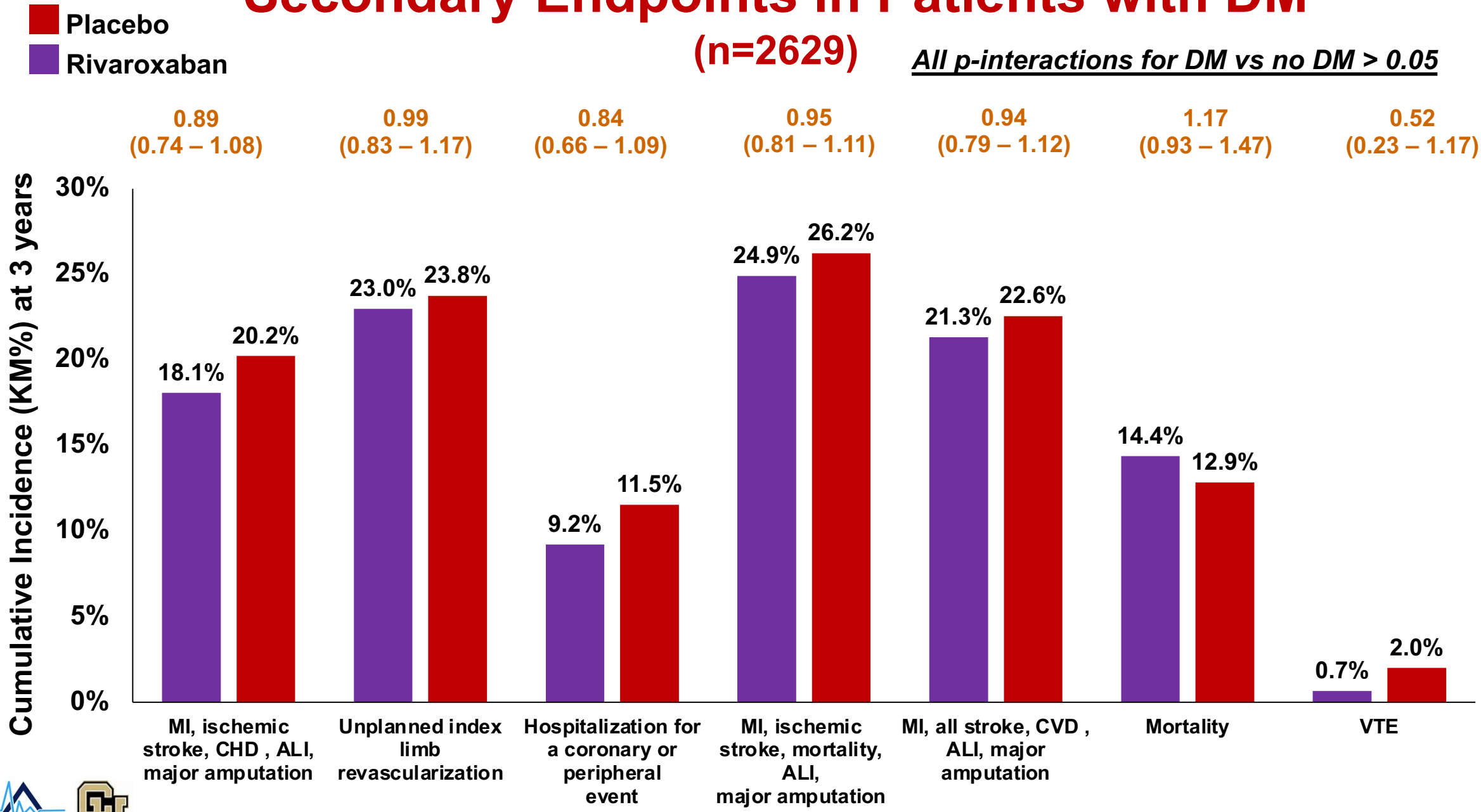
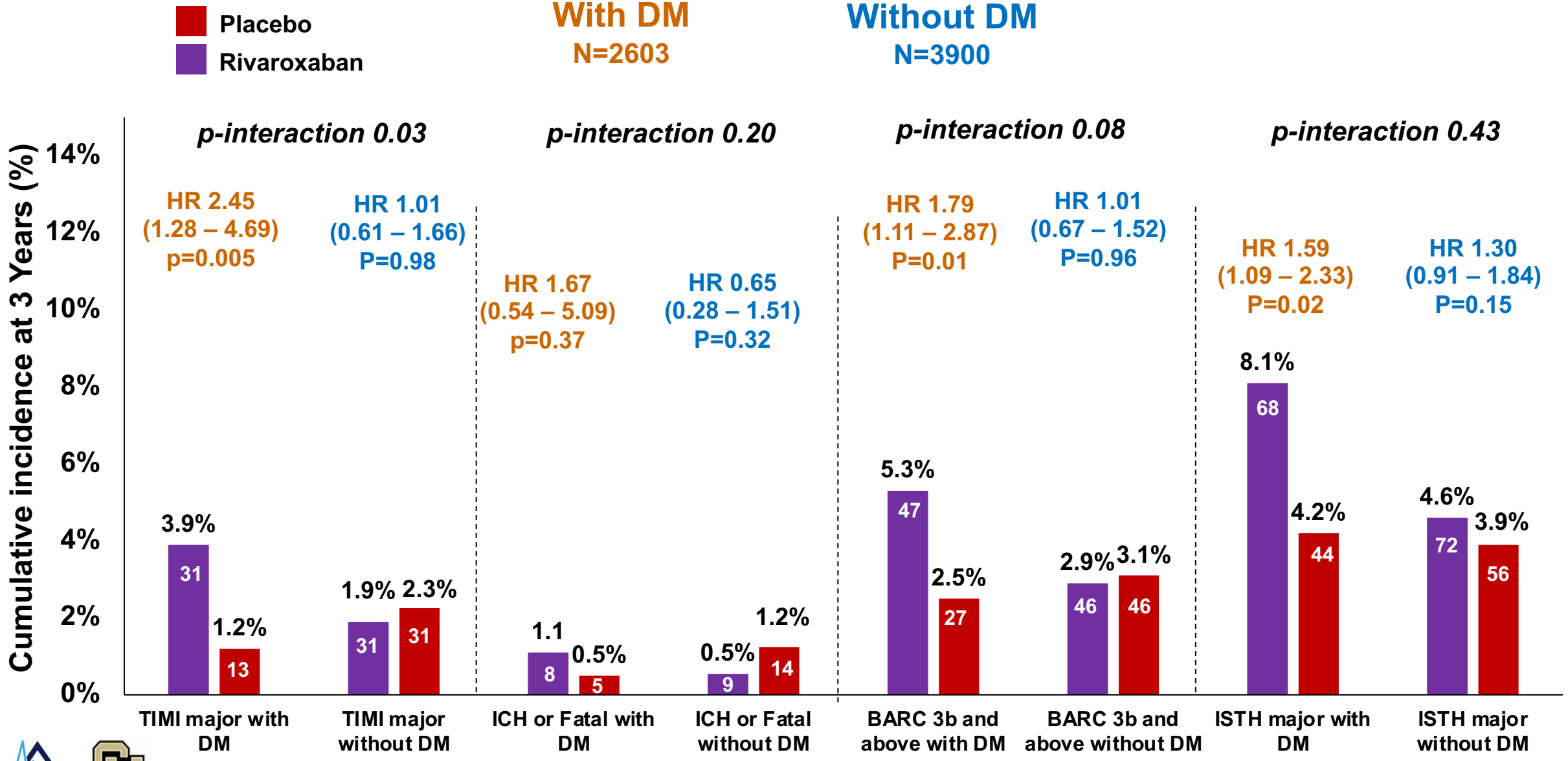
Secondary Endpoints in Patients with DM (n=2629)



Safety of Rivaroxaban by DM at Randomization



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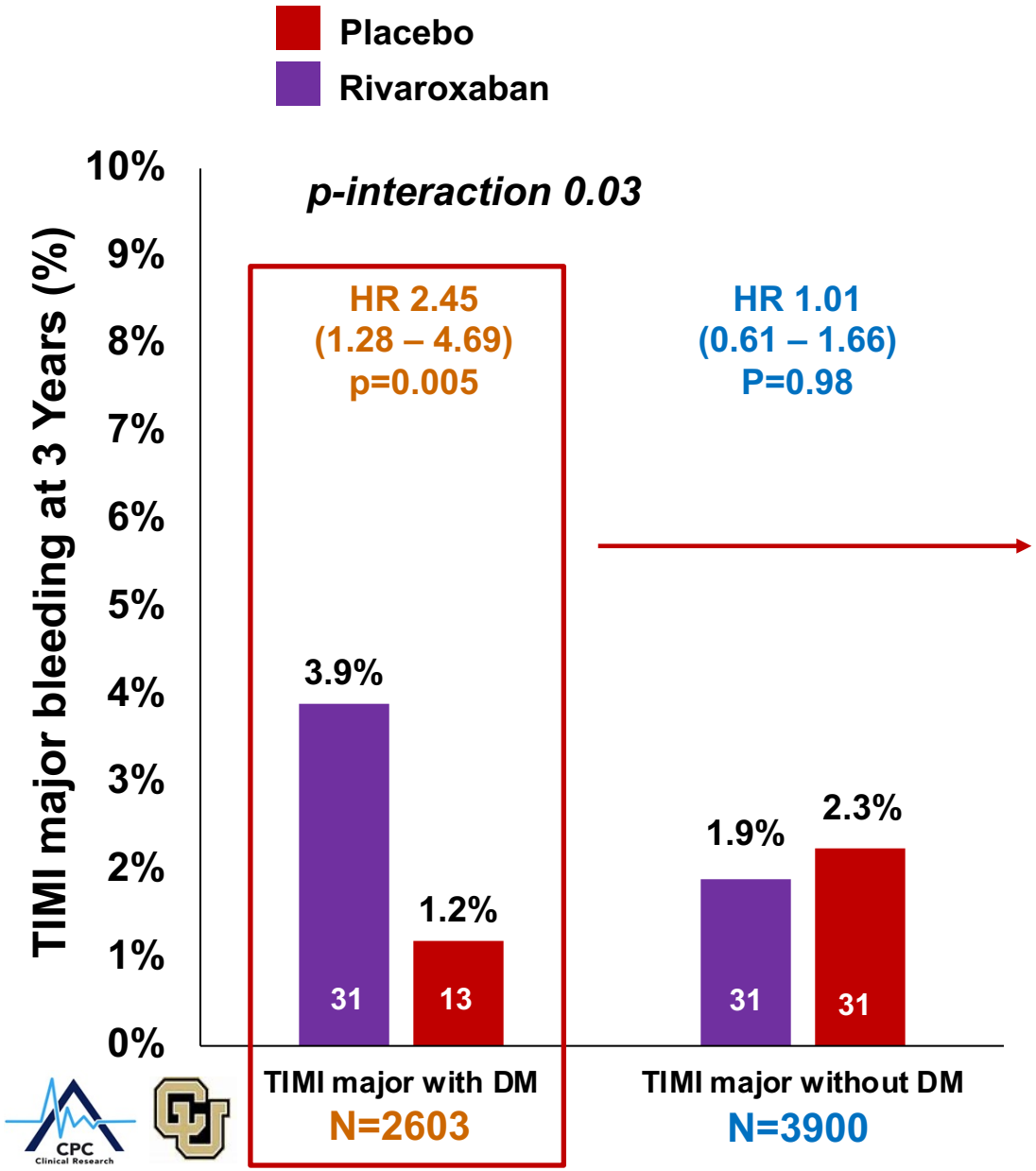
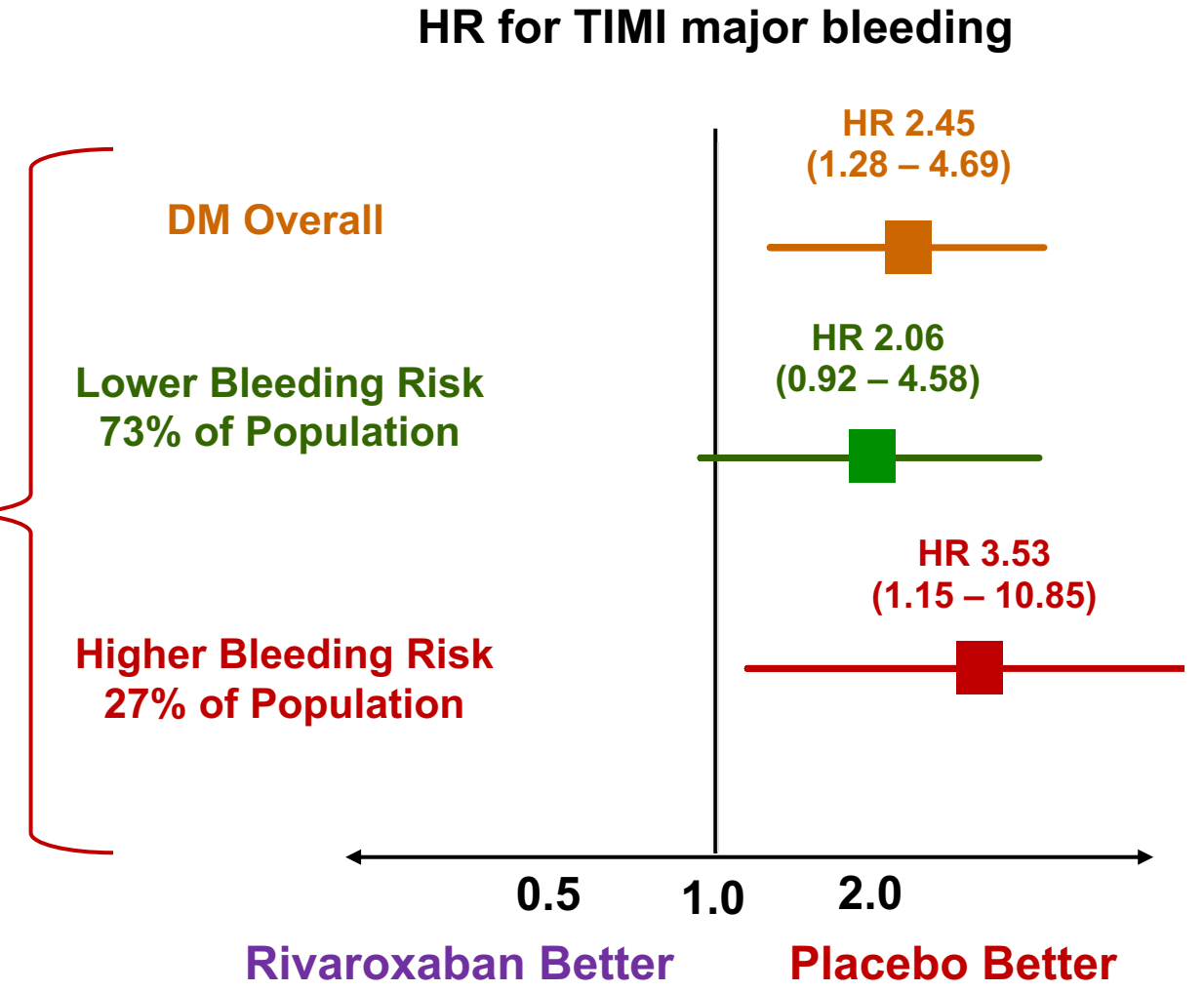
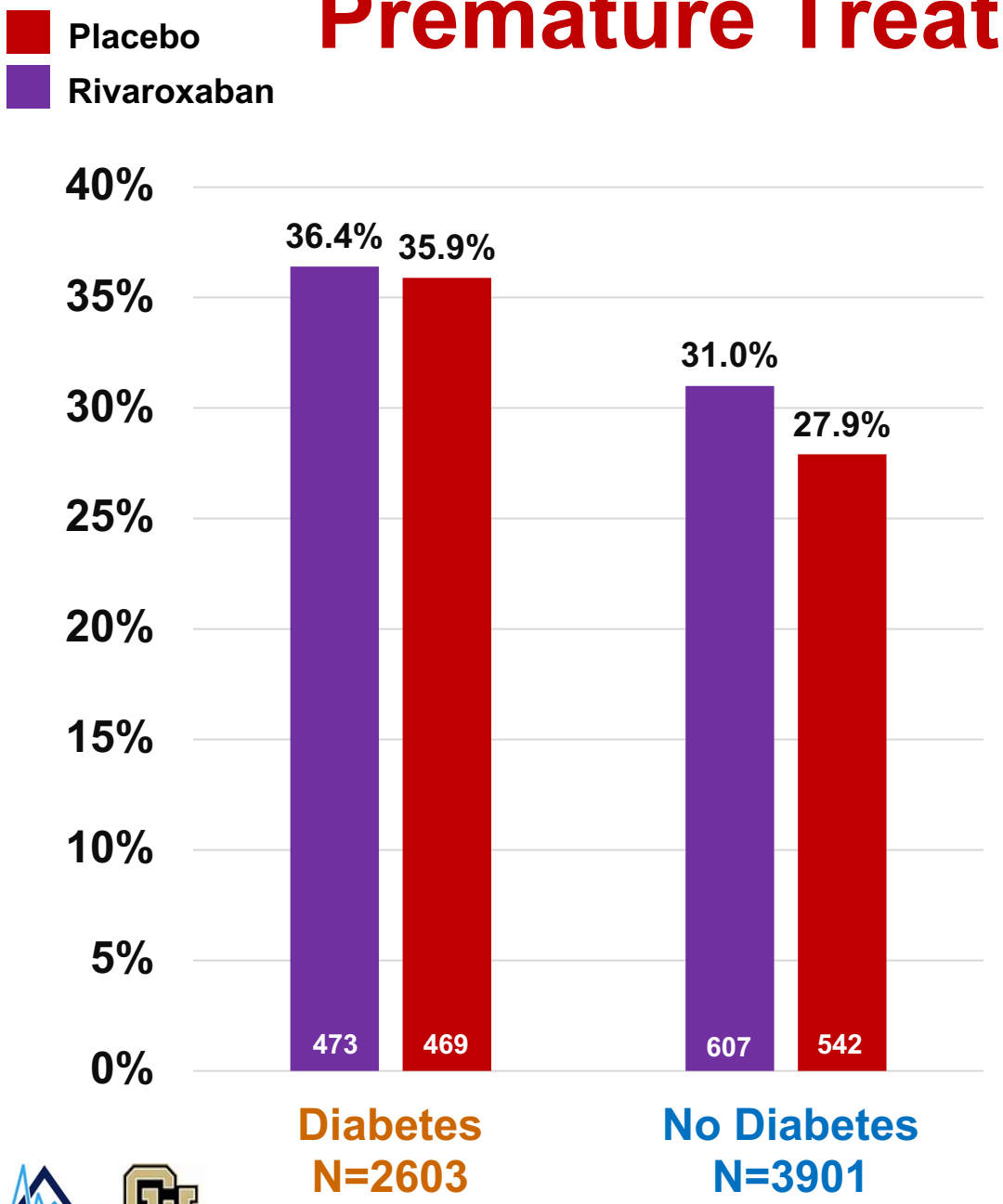
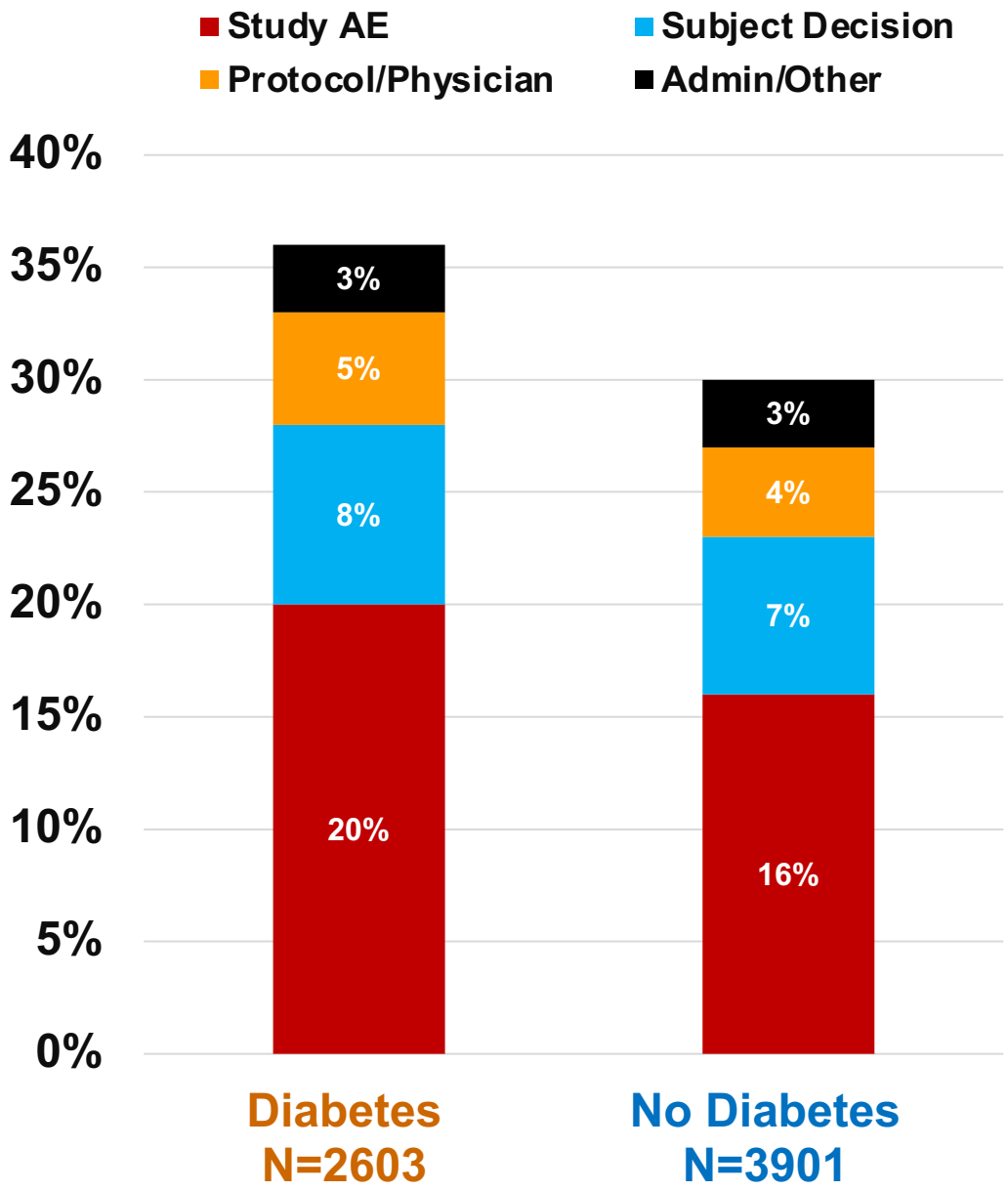




Higher Bleeding Risk = age ≥ 85 years or eGFR < 60 mL/min

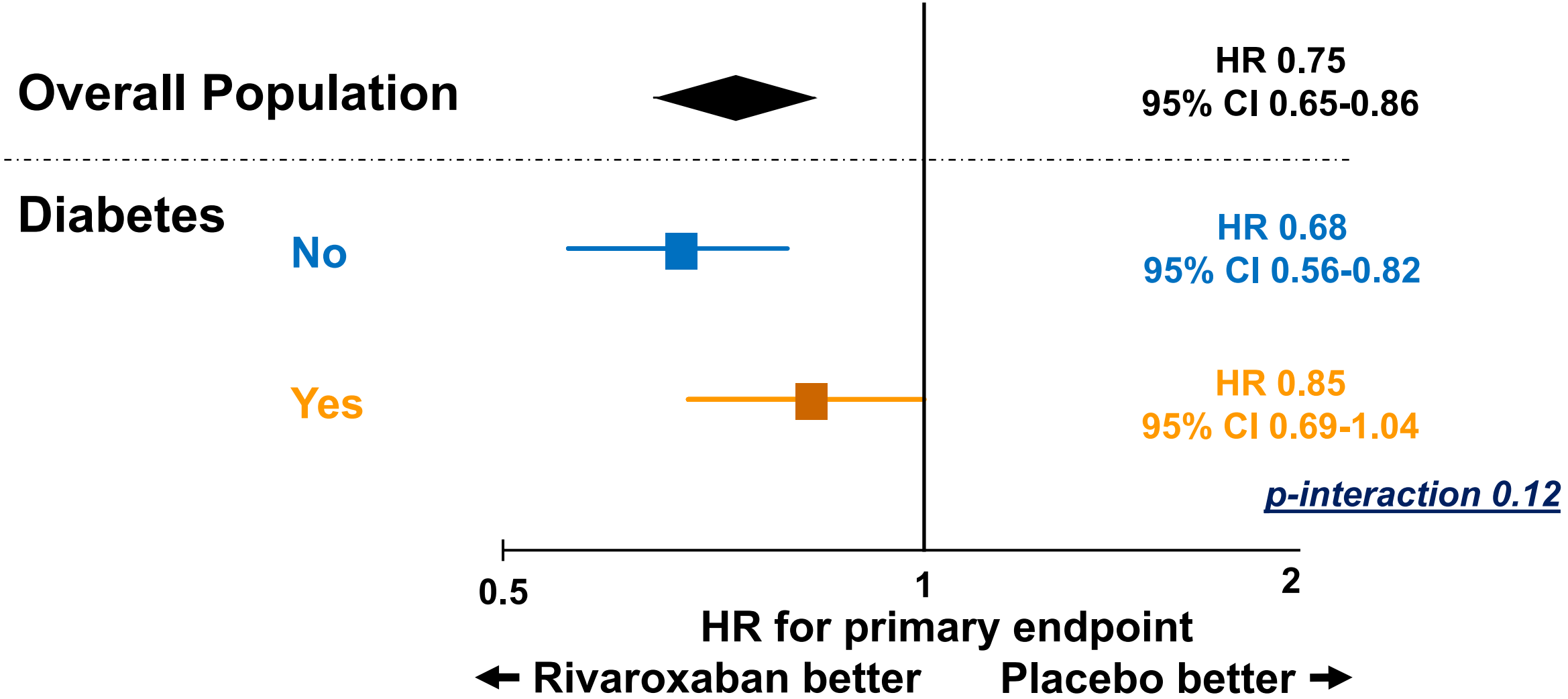
Premature Treatment Discontinuation





Primary Endpoint* in Patients With and Without Diabetes Mellitus

On Treatment



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Summary and Conclusions

- **Subjects with PAD with DM have a different baseline risk with more HTN, CAD, CLI, lower eGFR and more clopidogrel use, and are at extremely high risk of adverse events of the heart, limb, and brain after LER**
- **The efficacy of rivaroxaban 2.5 mg BID was consistent regardless of DM status at baseline, however a higher rate of discontinuation among these patients may have attenuated the observed benefit (ITT)**
- **Risk of TIMI major bleeding was greater in DM vs no DM, possibly driven by different baseline risk associated with bleeding and/or the low rate of bleeding observed in DM patients randomized to placebo (on ASA+/-clopi)**
- **Additional analyses are planned to understand the impact of competing risks (e.g. hospitalizations, all-cause mortality) to foster optimal patient selection for intensive prevention therapy**