

## SUPPLEMENTAL MATERIAL

**Table S1. Definition of Affected Arterial Bed**

	CAD	PAD	CVD
CRUSADE <sup>1</sup>	<ul style="list-style-type: none"> <li>Entire population presumed to have CAD</li> </ul>	<ul style="list-style-type: none"> <li>Amputation secondary to ischemia</li> <li>Current claudication</li> <li>Documentation of aortic aneurysm</li> <li>Lower extremity revascularization, such as vascular reconstruction, surgical bypass, percutaneous intervention)</li> <li>Positive non-invasive study, such as ABI &lt; 0.8</li> </ul>	<ul style="list-style-type: none"> <li>Prior stroke</li> </ul>
REACH <sup>2</sup>	<ul style="list-style-type: none"> <li>CABG</li> <li>MI</li> <li>PCI</li> <li>Stable angina</li> <li>Unstable angina</li> </ul>	<ul style="list-style-type: none"> <li>Claudication with prior intervention, such as amputation, angioplasty, atherectomy, peripheral bypass, stenting, or other vascular interventions</li> <li>Current claudication + ABI &lt; 0.9</li> </ul>	<ul style="list-style-type: none"> <li>Neurologist or hospital report of diagnosis of ischemic stroke or TIA</li> </ul>
CAPRIE <sup>3</sup>	<p>MI</p> <ul style="list-style-type: none"> <li>≤35 days prior to randomization <i>and</i></li> <li>Two of the following: <ul style="list-style-type: none"> <li>≥20 min ischemic chest pain</li> <li>Elevation CK-MB, LDH, or AST 2x upper limits of normal</li> <li>New Q waves in ≥2 adjacent ECG leads</li> <li>New dominant R wave in V1 (R ≥1 mm &gt; S in V1)</li> </ul> </li> </ul>	<ul style="list-style-type: none"> <li>Intermittent claudication of presumed atherosclerotic origin <i>and</i></li> <li>ABI ≤0.85 (two assessments on separate days) <i>or</i></li> <li>Intermittent claudication with prior leg amputation, reconstructive surgery, or angioplasty with no persisting complications from intervention</li> </ul>	<ul style="list-style-type: none"> <li>Focal neurologic deficit secondary of atherothrombotic origin Onset ≥1 week and ≤6 months before randomization <i>and</i></li> <li>Neurologic signs persisting ≥1 week from onset of stroke <i>and</i></li> <li>CT or MRI ruling out hemorrhage or non-relevant disease</li> </ul>
TRA2°P-TIMI 50 <sup>4</sup>	<ul style="list-style-type: none"> <li>History of spontaneous MI (excludes periprocedural or secondary MI)</li> </ul>	<ul style="list-style-type: none"> <li>Intermittent claudication and resting ABI &lt;0.85</li> <li>Prior amputation, peripheral bypass or angioplasty of extremities secondary to ischemia</li> </ul>	<ul style="list-style-type: none"> <li>Prior ischemic stroke</li> <li>Excludes hemorrhagic stroke</li> </ul>
PEGASUS-TIMI 54 <sup>5</sup>	<ul style="list-style-type: none"> <li>Entire population presumed to have CAD</li> </ul>	<ul style="list-style-type: none"> <li>ABI ≤0.90</li> <li>Prior peripheral revascularization</li> <li>Prior claudication</li> </ul>	<ul style="list-style-type: none"> <li>Prior ischemic stroke</li> </ul>
EUCLID <sup>6, 7</sup>	<ul style="list-style-type: none"> <li>Prior MI, PCI, or CABG</li> </ul>	<ul style="list-style-type: none"> <li>ABI ≤0.80 <ul style="list-style-type: none"> <li>Confirmation ABI of ≤0.85 required at randomization</li> </ul> </li> <li>If ABI was ≥1.40, a TBI cutoff of ≤0.60 was implemented</li> </ul>	<ul style="list-style-type: none"> <li>Prior stroke or TIA, carotid stenosis, or carotid revascularization</li> </ul>

		<ul style="list-style-type: none"> <li>○ Confirmation TBI of <math>\leq 0.65</math> required at randomization</li> <li>• Lower extremity revascularization &gt;30 days prior to randomization</li> </ul>	
SAVOR-TIMI 53 <sup>8</sup>	<ul style="list-style-type: none"> <li>• Prior MI that lead to hospitalization with final diagnosis of the following <ul style="list-style-type: none"> <li>○ MI</li> <li>○ PCI</li> <li>○ CABG or</li> </ul> </li> <li>• Objective evidence of CAD (<math>\geq 50\%</math> stenosis) in <math>\geq 2</math> arteries</li> </ul>	<ul style="list-style-type: none"> <li>• Intermittent claudication and ABI <math>&lt; 0.90</math> obtained in the previous 12 months</li> <li>• Prior peripheral revascularization or amputation of lower extremities at any level due to arterial obstructive disease (excludes amputations secondary infection and/or peripheral neuropathy)</li> </ul>	<ul style="list-style-type: none"> <li>• Prior acute focal neurologic deficit &gt;24 hours secondary to cerebral lesion of vascular origin. (excludes cardio-embolic events)</li> </ul>
LEADER <sup>9</sup>	<ul style="list-style-type: none"> <li>• Prior MI, PCI, or CABG</li> <li>• <math>\geq 50\%</math> coronary artery stenosis</li> <li>• Angina pectoris</li> <li>• Asymptomatic ischemia</li> </ul>	<ul style="list-style-type: none"> <li>• <math>\geq 50\%</math> peripheral artery stenosis</li> </ul>	<ul style="list-style-type: none"> <li>• Stroke</li> <li>• TIA</li> <li>• <math>\geq 50\%</math> intracranial or carotid artery stenosis</li> </ul>
IMPROVE-IT <sup>10</sup>	<ul style="list-style-type: none"> <li>• Entire population presumed to have CAD</li> </ul>	<ul style="list-style-type: none"> <li>• Claudication</li> <li>• Amputation</li> <li>• Vascular intervention of extremities</li> <li>• ABI <math>&lt; 0.80</math></li> <li>• Imaging evidence of <math>\geq 50\%</math> stenosis in extra coronary arterial bed</li> </ul>	<ul style="list-style-type: none"> <li>• Prior stroke or TIA</li> </ul>
FOURIER <sup>11, 12</sup>	<ul style="list-style-type: none"> <li>• Prior MI</li> </ul>	<ul style="list-style-type: none"> <li>• Intermittent claudication with ABI <math>&lt; 0.85</math></li> <li>• Peripheral vascular revascularization procedure</li> <li>• Amputation due atherosclerotic disease</li> </ul>	<ul style="list-style-type: none"> <li>• Prior stroke</li> </ul>
COMPASS <sup>13, 14</sup>	<ul style="list-style-type: none"> <li>• Previous MI</li> <li>• Stable angina or unstable angina with multi-vessel CAD (<math>&gt; 50\%</math> stenosis in <math>\geq 2</math> major coronary arteries, or positive stress test</li> <li>• Multi-vessel PCI</li> <li>• Multi-vessel CABG within 1 week or at least 4 years ago or with recurrent angina or ischemia any time after surgery</li> </ul>	<ul style="list-style-type: none"> <li>• Previous aorto-femoral bypass surgery, limb bypass surgery or percutaneous transluminal angioplasty of iliac or infrainguinal arteries</li> <li>• Previous limb or foot amputation for arterial vascular disease</li> <li>• Intermittent claudication with ABI <math>\leq 0.90</math> or significant peripheral artery stenosis (<math>&gt; 50\%</math>) documented by angiography or non-invasive testing by duplex ultrasound</li> <li>• Asymptomatic (no ipsilateral stroke or TIA within 6 months) carotid artery</li> </ul>	<ul style="list-style-type: none"> <li>• Not formally defined, but non-lacunar stroke <math>\geq 1</math> month prior to randomization was listed as an additional risk factor for inclusion</li> </ul>

		stenosis >50% as diagnosed by duplex ultrasound or angiography	
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ABI = ankle brachial index; AST = aspartate aminotransferase; CAD = coronary artery disease; CABG = coronary artery bypass graft; CAPRIE = Clopidogrel vs. Aspirin in Patients at Risk of Ischemic Events; CK = creatine kinase; COMPASS = Cardiovascular Outcomes for People Using Anticoagulation Strategies; CRUSADE = Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes with Early Implementation of the ACC/AHA Guidelines; CT = computed tomography; CVD = cerebral vascular disease; ECG = electrocardiogram; EUCLID = Effects of Ticagrelor and Clopidogrel in Patients with Peripheral Artery Disease; FOURIER = Further Cardiovascular Outcomes Research with PCSK9 Inhibition in Subjects with Elevated Risk; IMPROVE-IT = Improved Reduction of Outcomes: Vytorin Efficacy International Trial; LDH = lactate dehydrogenase; MI = myocardial infarction; LEADER = Liraglutide Effect and Action in Diabetes: Evaluation of Cardiovascular Results; MRI = magnetic resonance imaging; PAD = peripheral artery disease; PCI = percutaneous coronary artery intervention; PEGASUS-TIMI 54 = Patients With Prior Heart Attack Using Ticagrelor Compared to Placebo on a Background of Aspirin; REACH = Reduction of Atherothrombosis for Continued Health; SAVOR-TIMI 53 = Saxagliptin Assessment of Vascular Outcomes Recorded in Patients with Diabetes Mellitus – TIMI 53; TBI = toe-brachial index; TIA = transient ischemia attack; TRA2°P-TIMI 50 = Trial to Assess the Effects of Vorapaxar in Preventing Heart Attack and Stroke in Patients With Atherosclerosis – TIMI 50; UA = unstable angina

## Supplemental References

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