SUPPLEMENTAL MATERIAL

The Role of Combination Antiplatelet and Anticoagulation Therapy in Diabetes and Cardiovascular Disease: Insights from the COMPASS Trial

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Suppl. Table 1. Baseline characteristics of patients with and without diabetes at baseline in the entire trial.

	No Diabetes (N=17,054)	Diabetes (N=10,341)	P value
Age (year)	69.0±7.7	67.0±8.2	<0.0001
Female	3492 (20.5)	2528 (24.4)	<0.0001
Body mass index (kg/m^2)	27.7±4.3	29.3±5.2	<0.0001
Systolic blood pressure (mm Hg)	135±18	136±18	<0.0001
Diastolic blood pressure (mm Hg)	78±10	77±10	<0.0001
Total cholesterol (mmol/l)	4.2±1.0	4.1±1.1	<0.0001
Tobacco use			
Never	5457 (32.0)	3300 (31.9)	0.88
Former	8148 (47.8)	4623 (44.7)	<0.0001
Current	3449 (20.2)	2418 (23.4)	<0.0001
Hypertension	12108 (71.0)	8524 (82.4)	<0.0001
Previous stroke	514 (3.0)	518 (5.0)	<0.0001
Previous myocardial infarction	10838 (63.6)	6190 (59.9)	<0.0001
Heart failure	3476 (20.4)	2426 (23.5)	<0.0001
Coronary artery disease	15726 (92.2)	9098 (88.0)	<0.0001
Peripheral artery disease	4183 (24.5)	3287 (31.8)	<0.0001
Estimated GFR			
<30 ml/min	95 (0.6)	148 (1.4)	<0.0001
30 to <60 ml/min	3600 (21.1)	2433 (23.5)	<0.0001
≥60 ml/min	13354 (78.3)	7757 (75.0)	<0.0001
Race			
White	11508 (67.5)	5519 (53.4)	<0.0001
Black	114 (0.7)	148 (1.4)	<0.0001
Asian	2217 (13.0)	2052 (19.8)	<0.0001
Other	3215 (18.9)	2622 (25.4)	<0.0001
Geographic region			
North America	2441 (14.3)	1477 (14.3)	0.94
South America	3438 (20.2)	2706 (26.2)	<0.0001
Western Europe, Israel, Australia, or South Africa	6058 (35.5)	2497 (24.1)	<0.0001
Eastern Europe	3058 (17.9)	1765 (17.1)	0.07
Asia-Pacific	2059 (12.1)	1896 (18.3)	<0.0001
Medication			
ACE inhibitor or ARB	11826 (69.3)	7692 (74.4)	<0.0001
Calcium-channel blocker	4136 (24.3)	3133 (30.3)	<0.0001
Diuretic	4499 (26.4)	3640 (35.2)	<0.0001
Beta blocker	11883 (69.7)	7301 (70.6)	0.11
Lipid-lowering agent	15484 (90.8)	9117 (88.2)	<0.0001
NSAID	852 (5.0)	618 (6.0)	0.0005
Hypoglycemic agent	52 (0.3)	8503 (82.2)	<0.0001
Non-trial PPI	6167 (36.2)	3631 (35.1)	0.08

For continuous variables, plus-minus values are mean ± standard deviation. For categorical variables, frequency (percent) are shown.

P value is from the Wilcoxon 2-sample test for continuous variables, and Pearson chi-square test for categorical variables. GFR = glomerular filtration rate. ACE = angiotensin converting enzyme. ARB = angiotensin receptor blocker. NSAID = non-steroidal anti-inflammatory drug. PPI = proton pump inhibitor.

Suppl. Table 2. Baseline characteristics of patients with diabetes randomized to rivaroxaban plus aspirin or placebo plus aspirin.

	Rivaroxaban plus Aspirin (N=3,448)	Placebo plus Aspirin (N=3,474)	P value
Age (year)	66.9±8.3	67.0±8.2	0.84
Female	832 (24.1)	846 (24.4)	0.83
Body mass index (kg/m^2)	29.3±5.3	29.4±5.2	0.21
Systolic blood pressure (mm Hg)	136±17	136±17	0.57
Diastolic blood pressure (mm Hg)	77±10	77±10	0.99
Total cholesterol (mmol/l)	4.1±1.1	4.2±1.1	0.40
Tobacco use			
Never	1084 (31.4)	1139 (32.8)	0.23
Former	1559 (45.2)	1522 (43.8)	0.24
Current	805 (23.3)	813 (23.4)	0.96
Hypertension	2838 (82.3)	2857 (82.2)	0.94
Previous stroke	181 (5.2)	162 (4.7)	0.26
Previous myocardial infarction	2055 (59.6)	2100 (60.4)	0.47
Heart failure	780 (22.6)	834 (24.0)	0.17
Coronary artery disease	3043 (88.3)	3040 (87.5)	0.34
Peripheral artery disease	1100 (31.9)	1104 (31.8)	0.91
Estimated GFR			
<30 ml/min	50 (1.5)	49 (1.4)	0.89
30 to <60 ml/min	791 (22.9)	857 (24.7)	0.09
≥60 ml/min	2606 (75.6)	2568 (73.9)	0.11
Race			
White	1830 (53.1)	1878 (54.1)	0.41
Black	48 (1.4)	52 (1.5)	0.72
Asian	681 (19.8)	660 (19.0)	0.43
Other	889 (25.8)	884 (25.4)	0.75
Geographic region			
North America	495 (14.4)	502 (14.5)	0.91
South America	915 (26.5)	919 (26.5)	0.94
Western Europe, Israel, Australia, or South Africa	828 (24.0)	845 (24.3)	0.76
Eastern Europe	587 (17.0)	592 (17.0)	0.99
Asia-Pacific	623 (18.1)	616 (17.7)	0.71
Medication			
ACE inhibitor or ARB	2532 (73.4)	2569 (73.9)	0.63
Calcium-channel blocker	1059 (30.7)	1036 (29.8)	0.42
Diuretic	1209 (35.1)	1254 (36.1)	0.37
Beta blocker	2416 (70.1)	2450 (70.5)	0.68
Lipid-lowering agent	3028 (87.8)	3047 (87.7)	0.89
NSAID	223 (6.5)	203 (5.8)	0.28
Hypoglycemic agent	2820 (81.8)	2871 (82.6)	0.35
Non-trial PPI	1209 (35.1)	1203 (34.6)	0.70

For continuous variables, plus-minus values are mean ± standard deviation. For categorical variables, frequency (percent) are shown.

P value is from the Wilcoxon 2-sample test for continuous variables, and Pearson chi-square test for categorical variables. GFR = glomerular filtration rate. ACE = angiotensin converting enzyme. ARB = angiotensin receptor blocker. NSAID = non-steroidal anti-inflammatory drug. PPI = proton pump inhibitor.

Suppl. Table 3. Baseline characteristics of patients without diabetes randomized to rivaroxaban plus aspirin or placebo plus aspirin.

	Rivaroxaban plus Aspirin (N=5,704)	Placebo plus Aspirin (N=5,652)	P value
Age (year)	69.1±7.6	69.0±7.8	0.84
Female	1227 (21.5)	1143 (20.2)	0.09
Body mass index (kg/m^2)	27.7±4.3	27.8±4.3	0.96
Systolic blood pressure (mm Hg)	135±17	135±18	0.93
Diastolic blood pressure (mm Hg)	78±10	78±10	0.13
Total cholesterol (mmol/l)	4.2±1.0	4.2±1.0	0.72
Tobacco use			
Never	1838 (32.2)	1764 (31.2)	0.25
Former	2727 (47.8)	2729 (48.3)	0.61
Current	1139 (20.0)	1159 (20.5)	0.48
Hypertension	4069 (71.3)	4020 (71.1)	0.80
Previous stroke	170 (3.0)	173 (3.1)	0.80
Previous myocardial infarction	3599 (63.1)	3621 (64.1)	0.28
Heart failure	1183 (20.7)	1145 (20.3)	0.53
Coronary artery disease	5270 (92.4)	5221 (92.4)	0.97
Peripheral artery disease	1392 (24.4)	1400 (24.8)	0.65
Estimated GFR			
<30 ml/min	27 (0.5)	37 (0.7)	0.20
30 to <60 ml/min	1186 (20.8)	1171 (20.7)	0.91
≥60 ml/min	4488 (78.7)	4444 (78.6)	0.90
Race			
White	3843 (67.4)	3804 (67.3)	0.94
Black	28 (0.5)	40 (0.7)	0.13
Asian	770 (13.5)	737 (13.0)	0.47
Other	1063 (18.6)	1071 (18.9)	0.67
Geographic region			
North America	809 (14.2)	807 (14.3)	0.88
South America	1139 (20.0)	1135 (20.1)	0.88
Western Europe, Israel, Australia, or South Africa	2027 (35.5)	2010 (35.6)	0.98
Eastern Europe	1020 (17.9)	1012 (17.9)	0.97
Asia-Pacific	709 (12.4)	688 (12.2)	0.68
Medication			
ACE inhibitor or ARB	3943 (69.1)	3893 (68.9)	0.77
Calcium-channel blocker	1354 (23.7)	1446 (25.6)	0.02
Diuretic	1518 (26.6)	1492 (26.4)	0.80
Beta blocker	3973 (69.7)	3944 (69.8)	0.88
Lipid-lowering agent	5211 (91.4)	5111 (90.4)	0.09
NSAID	308 (5.4)	270 (4.8)	0.13
Hypoglycemic agent	20 (0.4)	15 (0.3)	0.41
Non-trial PPI	2059 (36.1)	2061 (36.5)	0.68

For continuous variables, plus-minus values are mean ± standard deviation. For categorical variables, frequency (percent) are shown.

P value is from the Wilcoxon 2-sample test for continuous variables, and Pearson chi-square test for categorical variables. GFR = glomerular filtration rate. ACE = angiotensin converting enzyme. ARB = angiotensin receptor blocker. NSAID = non-steroidal anti-inflammatory drug. PPI = proton pump inhibitor.

Suppl. Table 4. Outcomes in patients with diabetes by subgroups of PPI use at baseline for rivaroxaban plus aspirin versus placebo plus aspirin.

	Rivaroxaban plus Aspirin (N=3448)		Placebo plus Aspirin (N=3474)		Rivaroxaban plus Aspirin vs. Placebo plus Aspirin		
	No. of first events / patients (%)	Kaplan-Meier risk at 36 months	No. of first events / patients (%)	Kaplan-Meier risk at 36 months	Hazard Ratio (95% CI)	P value	P value for interaction*
Cardiovascular death, stroke, or myocardial infarction							
PPI use at baseline							0.32
Pantoprazole active	67 / 1116 (6.0)	8.6	74 / 1132 (6.5)	9.6	0.91 (0.65-1.27)	0.58	
Pantoprazole placebo	56 / 1124 (5.0)	9.9	85 / 1144 (7.4)	13.1	0.65 (0.46-0.91)	0.01	
Not randomized to PPI	56 / 1208 (4.6)	7.1	80 / 1198 (6.7)	9.7	0.68 (0.48-0.96)	0.03	
Major bleeding							
PPI use at baseline							0.88
Pantoprazole active	32 / 1116 (2.9)	4.1	18 / 1132 (1.6)	2.4	1.81 (1.02-3.23)	0.04	
Pantoprazole placebo	36 / 1124 (3.2)	4.6	20 / 1144 (1.7)	4.5	1.82 (1.05-3.14)	0.03	
Not randomized to PPI	42 / 1208 (3.5)	4.7	27 / 1198 (2.3)	3.6	1.55 (0.95-2.51)	0.07	
Cardiovascular death, stroke, myocardial infarction, fatal bleeding, or symptomatic bleeding into critical organ							
PPI use at baseline							0.12
Pantoprazole active	78 / 1116 (7.0)	9.7	78 / 1132 (6.9)	10.0	1.01 (0.74-1.39)	0.93	
Pantoprazole placebo	58 / 1124 (5.2)	9.9	90 / 1144 (7.9)	13.7	0.64 (0.46-0.89)	0.007	
Not randomized to PPI	68 / 1208 (5.6)	8.2	90 / 1198 (7.5)	11.7	0.74 (0.54-1.01)	0.06	

Percent (%) is the proportion of patients with an outcome.
Hazard ratios (95% CI) are from the stratified Cox proportional hazards regression models fit in the respective subgroup.
P values are from the stratified log-rank test.
*Test of interaction of relative risk reduction (Cox regression).