2.7.3.7 付録

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付表

表 2.7.3.7-1 人口統計学的特性及びベースライン特性（試験 17454、日本人集団、ITT）

	Rivaroxaban 2.5 mg bid + ASA 100 mg od N=230 (100%)	Rivaroxaban placebo bid + ASA 100 mg od N=229 (100%)	Total N=459 (100%)
Age (years)			
n	230	229	459
Nmiss	0	0	0
Mean	73.6	72.7	73.1
SD	7.6	8.0	7.8
Min	50	51	50
Q1	68.0	67.0	68.0
Median	73.0	73.0	73.0
Q3	79.0	78.0	79.0
Max	93	95	95
Age group (cut-offs: 55, 65, 75 years)			
<55 years	2 (0.9%)	7 (3.1%)	9 (2.0%)
55 - <65 years	21 (9.1%)	22 (9.6%)	43 (9.4%)
65 - 75 years	113 (49.1%)	122 (53.3%)	235 (51.2%)
>75 years	94 (40.9%)	78 (34.1%)	172 (37.5%)
Age group (cut-offs: 65, 75 years)			
<65 years	23 (10.0%)	29 (12.7%)	52 (11.3%)
>=65 to <75 years	100 (43.5%)	110 (48.0%)	210 (45.8%)
>=75 years	107 (46.5%)	90 (39.3%)	197 (42.9%)
Age group (cut-offs: 65, 85 years)			
<65 years	23 (10.0%)	29 (12.7%)	52 (11.3%)
>=65 to <85 years	193 (83.9%)	186 (81.2%)	379 (82.6%)
>=85 years	14 (6.1%)	14 (6.1%)	28 (6.1%)
Sex			
Male	178 (77.4%)	173 (75.5%)	351 (76.5%)
Female	52 (22.6%)	56 (24.5%)	108 (23.5%)
Days from qualifying revascularization procedure to randomization, actual			
n	230	229	459
Nmiss	0	0	0
Mean	4.5	4.9	4.7
SD	2.8	3.0	2.9
Min	1	1	1
Q1	2.0	2.0	2.0
Median	4.0	4.0	4.0
Q3	7.0	7.0	7.0
Max	11	11	11
Days from qualifying revascularization procedure to start of study drug, actual			
n	229	229	458
Nmiss	1	0	1
Mean	4.5	4.9	4.7
SD	2.8	3.0	2.9
Min	1	1	1
Q1	2.0	2.0	2.0
Median	4.0	4.0	4.0
Q3	7.0	8.0	7.0
Max	11	11	11

	Rivaroxaban 2.5 mg bid + ASA 100 mg od N=230 (100%)	Rivaroxaban placebo bid + ASA 100 mg od N=229 (100%)	Total N=459 (100%)
Type of procedure and clopidogrel use, per IxRS assignment			
SURGICAL	45 (19.6%)	44 (19.2%)	89 (19.4%)
Endovascular with clopidogrel	110 (47.8%)	110 (48.0%)	220 (47.9%)
Endovascular without clopidogrel	75 (32.6%)	75 (32.8%)	150 (32.7%)
Qualifying revascularization procedure per IxRS assignment			
Surgical	45 (19.6%)	44 (19.2%)	89 (19.4%)
Endovascular	185 (80.4%)	185 (80.8%)	370 (80.6%)
Type of qualifying procedure and clopidogrel use, actual			
Surgical	45 (19.6%)	41 (17.9%)	86 (18.7%)
Endovascular incl. hybrid with clopidogrel	108 (47.0%)	109 (47.6%)	217 (47.3%)
Endovascular incl. hybrid without clopidogrel	76 (33.0%)	78 (34.1%)	154 (33.6%)
Endovascular incl. hybrid with unknown clopidogrel use	1 (0.4%)	1 (0.4%)	2 (0.4%)
Actual type of qualifying procedure and clopidogrel use at randomization, detailed			
Endovascular incl. hybrid with clopidogrel	108 (47.0%)	109 (47.6%)	217 (47.3%)
Endovascular incl. hybrid without clopidogrel	76 (33.0%)	78 (34.1%)	154 (33.6%)
Endovascular incl. hybrid with unknown clopidogrel use	1 (0.4%)	1 (0.4%)	2 (0.4%)
Surgical with clopidogrel	7 (3.0%)	5 (2.2%)	12 (2.6%)
Surgical without clopidogrel	38 (16.5%)	36 (15.7%)	74 (16.1%)
Surgical with unknown clopidogrel use	0	0	0
Qualifying revascularization procedure, actual			
Surgical	45 (19.6%)	41 (17.9%)	86 (18.7%)
Endovascular incl. hybrid	185 (80.4%)	188 (82.1%)	373 (81.3%)
Qualifying revascularization procedure, actual (3 groups)			
Surgical	45 (19.6%)	41 (17.9%)	86 (18.7%)
Endovascular	177 (77.0%)	178 (77.7%)	355 (77.3%)
Hybrid	8 (3.5%)	10 (4.4%)	18 (3.9%)
Clopidogrel use in relation to qualifying revascularization procedure, actual			
No	98 (42.6%)	97 (42.4%)	195 (42.5%)
Yes	132 (57.4%)	131 (57.2%)	263 (57.3%)
Unknown	0	1 (0.4%)	1 (0.2%)
Clopidogrel use at the time of randomization			
No	114 (49.6%)	114 (49.8%)	228 (49.7%)
Yes	115 (50.0%)	114 (49.8%)	229 (49.9%)
Unknown	1 (0.4%)	1 (0.4%)	2 (0.4%)

	Rivaroxaban 2.5 mg bid + ASA 100 mg od N=230 (100%)	Rivaroxaban placebo bid + ASA 100 mg od N=229 (100%)	Total N=459 (100%)
Clopidogrel use continued after randomization (days) among clopidogrel user at randomization			
None	114 (49.6%)	114 (49.8%)	228 (49.7%)
<= 30 days	63 (27.4%)	63 (27.5%)	126 (27.5%)
> 30 days	51 (22.2%)	49 (21.4%)	100 (21.8%)
Unknown	2 (0.9%)	3 (1.3%)	5 (1.1%)
Weight group (cut-off 60 kg)			
missing	2 (0.9%)	1 (0.4%)	3 (0.7%)
<=60 kg	128 (55.7%)	136 (59.4%)	264 (57.5%)
>60 kg	100 (43.5%)	92 (40.2%)	192 (41.8%)
Baseline Estimated Glomerular Filtration Rate (mL/min/1.73m^2)			
n	230	229	459
Nmiss	0	0	0
Mean	64.395	67.696	66.041
SD	19.852	17.692	18.858
Min	27.00	24.10	24.10
Q1	50.800	55.500	53.440
Median	61.770	66.800	64.100
Q3	75.400	79.000	77.000
Max	154.60	123.00	154.60
eGFR (cut-offs: 60 ml/min/1.73m^2)			
missing	0	0	0
<60 ml/min/1.73m^2	106 (46.1%)	78 (34.1%)	184 (40.1%)
>=60 ml/min/1.73m^2	124 (53.9%)	151 (65.9%)	275 (59.9%)
eGFR (cut-offs: 15, 30 and 60 ml/min/1.73m^2)			
missing	0	0	0
<15 ml/min/1.73m^2	0	0	0
15 - <30 ml/min/1.73m^2	1 (0.4%)	4 (1.7%)	5 (1.1%)
30 - <60 ml/min/1.73m^2	105 (45.7%)	74 (32.3%)	179 (39.0%)
>=60 ml/min/1.73m^2	124 (53.9%)	151 (65.9%)	275 (59.9%)
eGFR (cut-offs: 30, 50 and 80 ml/min/1.73m^2)			
missing	0	0	0
<30 ml/min/1.73m^2	1 (0.4%)	4 (1.7%)	5 (1.1%)
30 - 50 ml/min/1.73m^2	54 (23.5%)	30 (13.1%)	84 (18.3%)
>50 - 80 ml/min/1.73m^2	128 (55.7%)	142 (62.0%)	270 (58.8%)
>80 ml/min/1.73m^2	47 (20.4%)	53 (23.1%)	100 (21.8%)
Fragile subjects			
missing	0	0	0
No	99 (43.0%)	107 (46.7%)	206 (44.9%)
Yes	131 (57.0%)	122 (53.3%)	253 (55.1%)

	Rivaroxaban 2.5 mg bid + ASA 100 mg od N=230 (100%)	Rivaroxaban placebo bid + ASA 100 mg od N=229 (100%)	Total N=459 (100%)
Baseline LDL Cholesterol (mmol/L)			
n	96	71	167
Nmiss	134	158	292
Mean	107.014	102.223	104.977
SD	34.454	30.900	32.979
Min	37.40	40.50	37.40
Q1	81.500	83.000	82.000
Median	103.000	96.000	97.000
Q3	129.500	119.000	128.000
Max	204.00	244.00	244.00
Smoking status			
missing	0	0	0
NEVER	40 (17.4%)	32 (14.0%)	72 (15.7%)
FORMER	126 (54.8%)	139 (60.7%)	265 (57.7%)
CURRENT	64 (27.8%)	58 (25.3%)	122 (26.6%)
Prior coronary artery disease			
missing	0	0	0
No	141 (61.3%)	149 (65.1%)	290 (63.2%)
Yes	89 (38.7%)	80 (34.9%)	169 (36.8%)
Prior MI			
missing	0	0	0
No	211 (91.7%)	212 (92.6%)	423 (92.2%)
Yes	19 (8.3%)	17 (7.4%)	36 (7.8%)
If yes, time of MI <12 months before randomization	0	5 (2.2%)	5 (1.1%)
Prior MI and eGFR < 60 mL/min/1.73m^2			
missing	211 (91.7%)	212 (92.6%)	423 (92.2%)
No	9 (3.9%)	10 (4.4%)	19 (4.1%)
Yes	10 (4.3%)	7 (3.1%)	17 (3.7%)
Prior MI and age <65 years			
missing	211 (91.7%)	212 (92.6%)	423 (92.2%)
No	15 (6.5%)	16 (7.0%)	31 (6.8%)
Yes	4 (1.7%)	1 (0.4%)	5 (1.1%)
Prior history of limb revascularization			
missing	0	0	0
No	128 (55.7%)	128 (55.9%)	256 (55.8%)
Yes	102 (44.3%)	101 (44.1%)	203 (44.2%)
Carotid artery disease history			
missing	0	0	0
No	207 (90.0%)	218 (95.2%)	425 (92.6%)
Yes	23 (10.0%)	11 (4.8%)	34 (7.4%)
Intermittent claudication present within past 12 months			
missing	0	0	0
No	3 (1.3%)	3 (1.3%)	6 (1.3%)
Yes	227 (98.7%)	226 (98.7%)	453 (98.7%)
History of heart failure			
missing	0	0	0
No	217 (94.3%)	219 (95.6%)	436 (95.0%)
Yes	13 (5.7%)	10 (4.4%)	23 (5.0%)

	Rivaroxaban 2.5 mg bid + ASA 100 mg od N=230 (100%)	Rivaroxaban placebo bid + ASA 100 mg od N=229 (100%)	Total N=459 (100%)
Diabetes mellitus			
missing	0	0	0
No	124 (53.9%)	120 (52.4%)	244 (53.2%)
Yes	106 (46.1%)	109 (47.6%)	215 (46.8%)
Hypertension			
missing	0	0	0
No	42 (18.3%)	40 (17.5%)	82 (17.9%)
Yes	188 (81.7%)	189 (82.5%)	377 (82.1%)
Hyperlipidemia			
missing	0	0	0
No	92 (40.0%)	92 (40.2%)	184 (40.1%)
Yes	138 (60.0%)	137 (59.8%)	275 (59.9%)
Baseline ABI (cut-off: 0.8)			
missing	7 (3.0%)	1 (0.4%)	8 (1.7%)
<= 0.8	44 (19.1%)	27 (11.8%)	71 (15.5%)
> 0.8	179 (77.8%)	201 (87.8%)	380 (82.8%)
Baseline TBI (cut-off: 0.6)			
missing	230 (100.0%)	229 (100.0%)	459 (100.0%)
<= 0.6	0	0	0
> 0.6	0	0	0
ABI/TBI categories at baseline (Month 1 visit)			
ABI <= 0.80 or TBI <= 0.60	44 (19.1%)	27 (11.8%)	71 (15.5%)
ABI > 0.80 and/or TBI > 0.60	179 (77.8%)	201 (87.8%)	380 (82.8%)
TBI and ABI not done	7 (3.0%)	1 (0.4%)	8 (1.7%)
Weight group (cut-offs: 70 and 90 kg)			
missing	2 (0.9%)	1 (0.4%)	3 (0.7%)
<=70 kg	196 (85.2%)	203 (88.6%)	399 (86.9%)
>70 - <=90 kg	31 (13.5%)	24 (10.5%)	55 (12.0%)
>90 kg	1 (0.4%)	1 (0.4%)	2 (0.4%)
Weight group (cut-off 50 kg)			
missing	2 (0.9%)	1 (0.4%)	3 (0.7%)
<50 kg	39 (17.0%)	51 (22.3%)	90 (19.6%)
>=50 kg	189 (82.2%)	177 (77.3%)	366 (79.7%)
Weight group (cut-offs: 50, 70 and 90 kg)			
missing	2 (0.9%)	1 (0.4%)	3 (0.7%)
<=50 kg	39 (17.0%)	52 (22.7%)	91 (19.8%)
50 - <=70 kg	157 (68.3%)	151 (65.9%)	308 (67.1%)
70 - <=90 kg	31 (13.5%)	24 (10.5%)	55 (12.0%)
>90 kg	1 (0.4%)	1 (0.4%)	2 (0.4%)
Creatinine Clearance Group (cut-offs: 30, 50, 80 mL/min)			
missing	2 (0.9%)	1 (0.4%)	3 (0.7%)
<30 mL/min	3 (1.3%)	8 (3.5%)	11 (2.4%)
30-<50 mL/min	71 (30.9%)	46 (20.1%)	117 (25.5%)
50-80 mL/min	109 (47.4%)	116 (50.7%)	225 (49.0%)
>80 mL/min	45 (19.6%)	58 (25.3%)	103 (22.4%)

	Rivaroxaban 2.5 mg bid + ASA 100 mg od N=230 (100%)	Rivaroxaban placebo bid + ASA 100 mg od N=229 (100%)	Total N=459 (100%)
Creatinine Clearance Group (cut-offs: 15, 30, 50, 80 mL/min)			
missing	2 (0.9%)	1 (0.4%)	3 (0.7%)
<15 mL/min	0	1 (0.4%)	1 (0.2%)
15-<30 mL/min	3 (1.3%)	7 (3.1%)	10 (2.2%)
30-<50 mL/min	71 (30.9%)	46 (20.1%)	117 (25.5%)
50-80 mL/min	109 (47.4%)	116 (50.7%)	225 (49.0%)
>80 mL/min	45 (19.6%)	58 (25.3%)	103 (22.4%)
Clopidogrel use in addition to baseline study ASA after randomization			
None	114 (49.6%)	114 (49.8%)	228 (49.7%)
>0 - <=30 days	63 (27.4%)	63 (27.5%)	126 (27.5%)
>30 - <=60 days	16 (7.0%)	19 (8.3%)	35 (7.6%)
>60 - <=180 days	24 (10.4%)	22 (9.6%)	46 (10.0%)
>180 days	11 (4.8%)	8 (3.5%)	19 (4.1%)
Unknown	2 (0.9%)	3 (1.3%)	5 (1.1%)
Atrial fibrillation disease history			
missing	0	0	0
No	224 (97.4%)	226 (98.7%)	450 (98.0%)
Yes	6 (2.6%)	3 (1.3%)	9 (2.0%)
Atrial flutter disease history			
missing	0	0	0
No	230 (100.0%)	229 (100.0%)	459 (100.0%)
Yes	0	0	0
Critical limb ischemia			
missing	0	0	0
No	197 (85.7%)	198 (86.5%)	395 (86.1%)
Yes	33 (14.3%)	31 (13.5%)	64 (13.9%)
Critical leg ischemia categories			
missing	0	0	0
No critical leg ischemia	197 (85.7%)	198 (86.5%)	395 (86.1%)
Critical leg ischemia history	15 (6.5%)	14 (6.1%)	29 (6.3%)
Critical leg ischemia ongoing	18 (7.8%)	17 (7.4%)	35 (7.6%)
Length of target lesion on the index leg			
missing	0	0	0
SHORT (< 5 CM)	70 (30.4%)	56 (24.5%)	126 (27.5%)
INTERMEDIATE (5 CM TO < 15 CM)	73 (31.7%)	82 (35.8%)	155 (33.8%)
LONG (>= 15 CM)	87 (37.8%)	91 (39.7%)	178 (38.8%)
Time from qualifying revascularization procedure to randomization, actual (cut-offs: median)			
< Median (Days)	132 (57.4%)	120 (52.4%)	252 (54.9%)
>= Median (Days)	98 (42.6%)	109 (47.6%)	207 (45.1%)
Statin use during study			
No	84 (36.5%)	84 (36.7%)	168 (36.6%)
Yes	146 (63.5%)	145 (63.3%)	291 (63.4%)
PAD symptom status (Rutherford score) (<=2, 3, >=4)			
missing	0	0	0
<=2	97 (42.2%)	107 (46.7%)	204 (44.4%)
3	106 (46.1%)	98 (42.8%)	204 (44.4%)
>=4	27 (11.7%)	24 (10.5%)	51 (11.1%)

	Rivaroxaban 2.5 mg bid + ASA 100 mg od N=230 (100%)	Rivaroxaban placebo bid + ASA 100 mg od N=229 (100%)	Total N=459 (100%)
PAD symptom status (Rutherford score) (<=2, 3, 4, >=5)			
missing	0	0	0
<=2	97 (42.2%)	107 (46.7%)	204 (44.4%)
3	106 (46.1%)	98 (42.8%)	204 (44.4%)
4	13 (5.7%)	11 (4.8%)	24 (5.2%)
>= 5	14 (6.1%)	13 (5.7%)	27 (5.9%)
Location of target lesion			
missing	45 (19.6%)	41 (17.9%)	86 (18.7%)
Aortoiliac region	2 (0.9%)	2 (0.9%)	4 (0.9%)
Femoropopliteal region	176 (76.5%)	180 (78.6%)	356 (77.6%)
Infrapopliteal artery region	6 (2.6%)	6 (2.6%)	12 (2.6%)
Other	1 (0.4%)	0	1 (0.2%)
Location of target lesion: Femoropopliteal region			
No	54 (23.5%)	49 (21.4%)	103 (22.4%)
Yes	176 (76.5%)	180 (78.6%)	356 (77.6%)
Qualifying endovascular technique: Balloon angioplasty			
No	95 (41.3%)	90 (39.3%)	185 (40.3%)
Yes	135 (58.7%)	139 (60.7%)	274 (59.7%)
Qualifying endovascular technique: Drug-coated balloon angioplasty			
No	229 (99.6%)	224 (97.8%)	453 (98.7%)
Yes	1 (0.4%)	5 (2.2%)	6 (1.3%)
Qualifying endovascular technique: Angioplasty with bare metal stent			
No	144 (62.6%)	150 (65.5%)	294 (64.1%)
Yes	86 (37.4%)	79 (34.5%)	165 (35.9%)
Qualifying endovascular technique: Angioplasty with drug-coated stent			
No	221 (96.1%)	222 (96.9%)	443 (96.5%)
Yes	9 (3.9%)	7 (3.1%)	16 (3.5%)
Qualifying endovascular technique: Angioplasty with covered stent			
No	222 (96.5%)	214 (93.4%)	436 (95.0%)
Yes	8 (3.5%)	15 (6.6%)	23 (5.0%)
Qualifying endovascular technique: Atherectomy			
No	230 (100.0%)	228 (99.6%)	458 (99.8%)
Yes	0	1 (0.4%)	1 (0.2%)
Qualifying endovascular technique: Thrombolysis			
No	229 (99.6%)	228 (99.6%)	457 (99.6%)
Yes	1 (0.4%)	1 (0.4%)	2 (0.4%)

	Rivaroxaban 2.5 mg bid + ASA 100 mg od N=230 (100%)	Rivaroxaban placebo bid + ASA 100 mg od N=229 (100%)	Total N=459 (100%)
Endovascular qualifying procedure with drug coated devices			
missing	45 (19.6%)	41 (17.9%)	86 (18.7%)
Drug-coated balloon or drug-coated stent	10 (4.3%)	12 (5.2%)	22 (4.8%)
Not drug-coated devices	175 (76.1%)	176 (76.9%)	351 (76.5%)
No device	0	0	0

The ITT analysis set includes all randomized subjects.
For the total ITT analysis set the median time from actual qualifying revascularization to randomization is 5 days.
bid = twice daily, od = once daily, ASA = acetylsalicylic acid
eGFR = estimated glomerular filtration rate, ABI = ankle brachial index, TBI = toe brachial index, LDL = low-density lipoprotein, MI = myocardial infarction
Percentages are calculated with the number of subjects in each parameter and treatment group as denominator.
Subjects are considered fragile if age >75 years or weight <=50 kg or baseline eGFR <50 mL/min/1.73m2. Subgroup variables from Atrial fibrillation disease history and below are added post-hoc.
Baseline value for ABI and TBI is defined as the measurement at month 1 visit. All other baseline characteristics are defined as the measurement at screening.

Source: 5.3.5.1.2 17454_J_analysis/Table 14.1.2/1

表 2.7.3.7-2 血行再建術のタイプ及びクロピドグレル使用の有無に関する IxRS による層別内容及び実際の治療内容の分布（試験 17454、日本人集団、ITT）

	Actual				
Per IxRS assignment	Endovascular Incl. Hybrid with Unknown Clopidogrel Use	Endovascular Incl. Hybrid with Clopidogrel	Endovascular Incl. Hybrid without Clopidogrel	Surgical	Total
Endovascular with Clopidogrel	2 (0.91%)	**209 (95%)**	9 (4.09%)	0 (0%)	220 (100%)
Endovascular without Clopidogrel	0 (0%)	6 (4%)	**140 (93.33%)**	4 (2.67%)	150 (100%)
Surgery	0 (0%)	2 (2.25%)	5 (5.62%)	**82 (92.13%)**	89 (100%)
Total	2 (0.44%)	217 (47.28%)	154 (33.55%)	86 (18.74%)	459 (100%)

The ITT analysis set includes all randomized subjects.
Per IxRS assignment: recorded in IxRS system (based on investigator's input of type of procedure and clopidogrel use at the time of randomization).
Actual: Determined by the actual index revascularization procedure the subject received and any clopidogrel use at the time of randomization from the electronic case report forms.
Percentages are calculated with the total number of subjects in each row as the denominator
bid = twice daily, od = once daily, ASA = acetylsalicylic acid

Source: 5.3.5.1.2 17454_J_analysis/Table 14.1.5/12

表 2.7.3.7-3 試験への組入れの根拠とした血行再建術施行前の PAD の重症度（試験 17454、日本人集団、ITT）

Symptom Classification	Rivaroxaban 2.5 mg bid + ASA 100 mg od N=230 (100%)	Rivaroxaban placebo bid + ASA 100 mg od N=229 (100%)	Total N=459 (100%)
Asymptomatic (exclusionary) (0)	0	0	0
Mild claudication with no limitation in walking (exclusionary) (1)	0	0	0
Mild to moderate claudication (2)	80 (34.8%)	81 (35.4%)	161 (35.1%)
Severe claudication (3)	86 (37.4%)	83 (36.2%)	169 (36.8%)
Ischemic rest pain (4)	12 (5.2%)	9 (3.9%)	21 (4.6%)
Ischemic ulceration not exceeding ulcers of the digits of the foot (5)	12 (5.2%)	7 (3.1%)	19 (4.1%)
Ischemic ulceration or gangrene exceeding minimal gangrene of the toes (exclusionary) (6)	1 (0.4%)	1 (0.4%)	2 (0.4%)
missing	39 (17.0%)	48 (21.0%)	87 (19.0%)

The ITT analysis set includes all randomized subjects.
bid = twice daily, od = once daily, ASA = acetylsalicylic acid
Symptoms are recorded using stages (0-6) of Rutherford classification.
Subjects with multiple PAD symptoms prior to qualifying revascularization are counted only once, in the most severe category
Source: 5.3.5.1.2 17454_J_analysis/Table 14.1.2/9

表 2.7.3.7-4 実際に行われた血行再建術のタイプ及びクロピドグレル使用の有無別による治験薬及び試験用 ASA の投与期間（試験 17454、日本人集団、SAF）

	Rivaroxaban 2.5 mg bid + ASA 100 mg od			Rivaroxaban placebo bid + ASA 100 mg od		
	Surgical	Endovascular with clopidogrel	Endovascular without clopidogrel	Surgical	Endovascular with clopidogrel	Endovascular without clopidogrel
	N=45 (100%)	N=108 (100%)	N=75 (100%)	N=41 (100%)	N=109 (100%)	N=78 (100%)
Total rivaroxaban/rivaroxaban placebo treatment duration (months)						
≤ 3	2 (4.4%)	10 (9.3%)	6 (8.0%)	1 (2.4%)	3 (2.8%)	2 (2.6%)
> 3 - ≤ 6	2 (4.4%)	4 (3.7%)	1 (1.3%)	3 (7.3%)	5 (4.6%)	2 (2.6%)
> 6 - ≤ 9	2 (4.4%)	2 (1.9%)	2 (2.7%)	2 (4.9%)	4 (3.7%)	4 (5.1%)
> 9 - ≤ 12	1 (2.2%)	1 (0.9%)	3 (4.0%)	0	3 (2.8%)	0
> 12 - ≤ 18	4 (8.9%)	8 (7.4%)	2 (2.7%)	2 (4.9%)	8 (7.3%)	6 (7.7%)
> 18 - ≤ 24	7 (15.6%)	24 (22.2%)	16 (21.3%)	4 (9.8%)	23 (21.1%)	18 (23.1%)
> 24	27 (60.0%)	59 (54.6%)	45 (60.0%)	29 (70.7%)	63 (57.8%)	46 (59.0%)
Total rivaroxaban/rivaroxaban placebo treatment duration (days)						
n	45	108	75	41	109	78
Mean	760.1	743.9	748.5	805.7	756.6	776.1
SD	356.4	368.2	331.0	341.3	323.1	309.4
Min	4	3	7	26	6	28
Median	775.0	759.5	792.0	835.0	783.0	782.0
Max	1337	1424	1254	1334	1435	1372
Time on rivaroxaban/rivaroxaban placebo (excluding days off study drug, days)						
n	45	108	75	41	109	78
Mean	748.4	727.9	740.3	789.7	746.9	764.2
SD	354.6	361.6	329.4	335.7	322.7	305.4
Min	4	3	7	26	6	27
Median	769.0	742.0	792.0	834.0	771.0	778.0
Max	1337	1424	1254	1334	1435	1372
Total ASA treatment duration (months)						
≤ 3	3 (6.7%)	6 (5.6%)	6 (8.0%)	1 (2.4%)	4 (3.7%)	2 (2.6%)
> 3 - ≤ 6	2 (4.4%)	4 (3.7%)	1 (1.3%)	2 (4.9%)	4 (3.7%)	1 (1.3%)
> 6 - ≤ 9	1 (2.2%)	2 (1.9%)	0	1 (2.4%)	4 (3.7%)	3 (3.8%)
> 9 - ≤ 12	1 (2.2%)	1 (0.9%)	2 (2.7%)	0	3 (2.8%)	2 (2.6%)
> 12 - ≤ 18	3 (6.7%)	7 (6.5%)	1 (1.3%)	1 (2.4%)	8 (7.3%)	3 (3.8%)
> 18 - ≤ 24	7 (15.6%)	26 (24.1%)	16 (21.3%)	4 (9.8%)	24 (22.0%)	16 (20.5%)
> 24	28 (62.2%)	62 (57.4%)	49 (65.3%)	32 (78.0%)	62 (56.9%)	51 (65.4%)
Total ASA treatment duration (days)						
n	45	108	75	41	109	78
Mean	780.0	778.8	778.3	876.1	756.5	806.0
SD	369.9	345.2	313.2	323.2	328.6	295.4
Min	3	14	7	25	5	28
Median	779.0	774.0	796.0	891.0	777.0	806.0
Max	1337	1423	1254	1334	1434	1372
Time on ASA (excluding days off study ASA, days)						
n	45	108	75	41	109	78
Mean	758.8	762.8	768.1	858.7	750.2	800.0
SD	357.8	341.3	312.8	317.5	328.7	294.6
Min	3	14	7	25	5	28
Median	773.0	763.5	796.0	886.0	771.0	805.5
Max	1337	1423	1253	1334	1434	1372

Treatment duration = date of last study drug or study ASA - date of first study drug or study ASA + 1 day.
ASA = acetylsalicylic acid, bid = twice daily, Max = maximum, Min = minimum, od = once daily, SAF = safety analysis set, SD = standard deviation
Source: 5.3.5.1.2 17454_J_analysis/Table 14.1.5/2, 14.1.5/4

表 2.7.3.7-5 試験期間（試験 17454、日本人集団、ITT）

	Rivaroxaban 2.5 mg bid + ASA 100 mg od N=230 (100%)	Rivaroxaban placebo bid + ASA 100 mg od N=229 (100%)	Total N=459 (100%)
Time from randomization to death or date of last contact alive (month)			
<= 3 months	5 (2.2%)	1 (0.4%)	6 (1.3%)
> 3 months -<= 6 months	1 (0.4%)	0	1 (0.2%)
> 6 months -<= 9 months	1 (0.4%)	4 (1.7%)	5 (1.1%)
> 9 months -<= 12 months	0	5 (2.2%)	5 (1.1%)
> 12 months -<= 18 months	1 (0.4%)	5 (2.2%)	6 (1.3%)
> 18 months -<= 24 months	41 (17.8%)	37 (16.2%)	78 (17.0%)
> 24 months	181 (78.7%)	177 (77.3%)	358 (78.0%)
Time from randomization to death or date of last contact alive (days)			
n	230	229	459
Mean	920.8	904.1	912.5
SD	267.3	262.0	264.5
Min	1	53	1
Q1	739.0	736.0	737.0
Median	888.5	874.0	883.0
Q3	1135.0	1098.0	1121.0
Max	1456	1465	1465
Time from randomization to death or date of last contact alive until ECOD (month)			
<= 3 months	5 (2.2%)	1 (0.4%)	6 (1.3%)
> 3 months -<= 6 months	1 (0.4%)	0	1 (0.2%)
> 6 months -<= 9 months	1 (0.4%)	4 (1.7%)	5 (1.1%)
> 9 months -<= 12 months	0	5 (2.2%)	5 (1.1%)
> 12 months -<= 18 months	1 (0.4%)	5 (2.2%)	6 (1.3%)
> 18 months -<= 24 months	56 (24.3%)	50 (21.8%)	106 (23.1%)
> 24 months	166 (72.2%)	164 (71.6%)	330 (71.9%)
Time from randomization to death or date of last contact alive until ECOD (days)			
n	230	229	459
Mean	890.6	873.8	882.2
SD	264.7	257.5	261.0
Min	1	53	1
Q1	706.0	698.0	703.0
Median	863.0	843.0	851.0
Q3	1099.0	1063.0	1081.0
Max	1398	1424	1424
Time from randomization until earlier of LCEAD or ECOD (month)			
<= 3 months	5 (2.2%)	1 (0.4%)	6 (1.3%)
> 3 months -<= 6 months	1 (0.4%)	1 (0.4%)	2 (0.4%)
> 6 months -<= 9 months	1 (0.4%)	4 (1.7%)	5 (1.1%)
> 9 months -<= 12 months	0	5 (2.2%)	5 (1.1%)
> 12 months -<= 18 months	1 (0.4%)	7 (3.1%)	8 (1.7%)
> 18 months -<= 24 months	56 (24.3%)	50 (21.8%)	106 (23.1%)
> 24 months	166 (72.2%)	161 (70.3%)	327 (71.2%)
Time from randomization until earlier of LCEAD or ECOD (days)			
n	230	229	459
Mean	889.9	866.5	878.2
SD	265.1	262.9	264.0
Min	1	53	1
Q1	706.0	696.0	698.0
Median	861.0	832.0	843.0
Q3	1099.0	1062.0	1081.0
Max	1398	1424	1424

The ITT analysis set includes all randomized subjects.
ECOD=efficacy cut-off date, Efficacy cut-off date = 08SEP2019; LCEAD=last clinical event ascertainment date
bid = twice daily, od = once daily, ASA = acetylsalicylic acid
Source: 5.3.5.1.2 17454_J_analysis/Table 14.1.1/12

表 2.7.3.7-6 ECOD までにリバーロキサバン/プラセボ又は試験用 ASA の投与を中止した被験者の割合（試験 17454、無作為割付け時のクロピドグレル使用の有無別、全体集団、SAF）

Disposition	Rivaroxaban 2.5 mg bid + ASA 100 mg od	Rivaroxaban placebo bid + ASA 100 mg od
Clopidogrel use: No		
Premature permanent discontinuation of **rivaroxaban/rivaroxaban placebo**		
Overall	**517/1603 (32.3%)**	**461/1601 (28.8%)**
Surgical	273/ 918 (29.7%)	256/ 938 (27.3%)
Endovascular with clopidogrel	0	0
Endovascular without clopidogrel	244/ 685 (35.6%)	205/ 663 (30.9%)
Premature permanent discontinuation of **ASA**		
Overall	**450/1603 (28.1%)**	**412/1601 (25.7%)**
Surgical	230/ 918 (25.1%)	221/ 938 (23.6%)
Endovascular with clopidogrel	0	0
Endovascular without clopidogrel	220/ 685 (32.1%)	191/ 663 (28.8%)
Clopidogrel use: Yes		
Premature permanent discontinuation of **rivaroxaban/rivaroxaban placebo**		
Overall	**562/1646 (34.1%)**	**547/1637 (33.4%)**
Surgical	50/ 151 (33.1%)	39/ 156 (25.0%)
Endovascular with clopidogrel	512/1495 (34.2%)	508/1481 (34.3%)
Endovascular without clopidogrel	0	0
Premature permanent discontinuation of **ASA**		
Overall	**491/1646 (29.8%)**	**478/1637 (29.2%)**
Surgical	43/ 151 (28.5%)	32/ 156 (20.5%)
Endovascular with clopidogrel	448/1495 (30.0%)	446/1481 (30.1%)
Endovascular without clopidogrel	0	0

ASA = acetylsalicylic acid, bid = twice daily, od = once daily, SAF = safety analysis set.

Source: 5.3.5.1.1 PH-40161/Post-hoc Table 14.3.5.4.2/1, 14.3.5.4.2/2, 14.3.5.4.2/4, 14.3.5.4.2/5

表 2.7.3.7-7 病歴（試験 17454、日本人集団、ITT）

	Rivaroxaban 2.5 mg bid + ASA 100 mg od N=230 (100%)	Rivaroxaban placebo bid + ASA 100 mg od N=229 (100%)	Total N=459 (100%)
Coronary artery history			
Coronary artery disease	89 (38.7%)	80 (34.9%)	169 (36.8%)
If yes, known coronary stenosis in at least one coronary bed >=50%	89 (38.7%)	78 (34.1%)	167 (36.4%)
No	13 (5.7%)	14 (6.1%)	27 (5.9%)
Yes	76 (33.0%)	64 (27.9%)	140 (30.5%)
Angina pectoris	57 (24.8%)	50 (21.8%)	107 (23.3%)
Myocardial infarction	19 (8.3%)	17 (7.4%)	36 (7.8%)
If yes, type			
missing	0	0	0
NSTEMI	2 (0.9%)	2 (0.9%)	4 (0.9%)
STEMI	7 (3.0%)	9 (3.9%)	16 (3.5%)
UNKNOWN	10 (4.3%)	6 (2.6%)	16 (3.5%)
Valvular heart disease history			
Valvular heart disease	12 (5.2%)	9 (3.9%)	21 (4.6%)
If yes, severity			
missing	0	0	0
MILD	9 (3.9%)	6 (2.6%)	15 (3.3%)
MODERATE	3 (1.3%)	1 (0.4%)	4 (0.9%)
SEVERE	0	2 (0.9%)	2 (0.4%)
Atrial fibrillation disease history			
Atrial fibrillation disease (any prior history)	6 (2.6%)	3 (1.3%)	9 (2.0%)
Atrial flutter disease history			
Atrial flutter disease (any prior history)	0	0	0
Percutaneous coronary intervention history			
Percutaneous coronary intervention	53 (23.0%)	38 (16.6%)	91 (19.8%)
If yes, type of procedure			
missing	1 (0.4%)	0	1 (0.2%)
BIOABSORBABLE STENT	0	0	0
BMS	2 (0.9%)	3 (1.3%)	5 (1.1%)
DEBULKING	0	0	0
PROCEDURE/ATHERECTOMY			
DES	43 (18.7%)	30 (13.1%)	73 (15.9%)
OTHER	1 (0.4%)	0	1 (0.2%)
PTCA ONLY	6 (2.6%)	5 (2.2%)	11 (2.4%)
Coronary artery bypass graft history			
Coronary artery bypass graft	16 (7.0%)	14 (6.1%)	30 (6.5%)
Coronary artery bypass graft, IMA	5 (2.2%)	5 (2.2%)	10 (2.2%)
Coronary artery bypass graft, >= 3 vessel bypass grafting	9 (3.9%)	9 (3.9%)	18 (3.9%)
Heart failure history			
Heart failure	13 (5.7%)	10 (4.4%)	23 (5.0%)
If yes, type			
missing	0	0	0
NYHA CLASS I	8 (3.5%)	9 (3.9%)	17 (3.7%)
NYHA CLASS II	2 (0.9%)	1 (0.4%)	3 (0.7%)
NYHA CLASS III	2 (0.9%)	0	2 (0.4%)
NYHA CLASS IV	1 (0.4%)	0	1 (0.2%)
Pacemaker history			
Pacemaker	1 (0.4%)	4 (1.7%)	5 (1.1%)
Defibrillator (ICD)	1 (0.4%)	1 (0.4%)	2 (0.4%)
Cerebrovascular history			
Carotid artery disease			
Carotid artery stenosis of >= 50%	21 (9.1%)	10 (4.4%)	31 (6.8%)
Carotid endarterectomy	2 (0.9%)	1 (0.4%)	3 (0.7%)
If yes, laterality			
missing	0	0	0
BILATERAL	0	0	0
LEFT	1 (0.4%)	0	1 (0.2%)
RIGHT	1 (0.4%)	1 (0.4%)	2 (0.4%)

	Rivaroxaban 2.5 mg bid + ASA 100 mg od N=230 (100%)	Rivaroxaban placebo bid + ASA 100 mg od N=229 (100%)	Total N=459 (100%)
Percutaneous carotid intervention	5 (2.2%)	2 (0.9%)	7 (1.5%)
If yes, laterality			
missing	0	0	0
BILATERAL	0	0	0
LEFT	2 (0.9%)	1 (0.4%)	3 (0.7%)
RIGHT	3 (1.3%)	1 (0.4%)	4 (0.9%)
Peripheral vascular history			
Claudication	227 (98.7%)	226 (98.7%)	453 (98.7%)
If yes, claudication present within past 12 months?	227 (98.7%)	226 (98.7%)	453 (98.7%)
No	0	0	0
Yes	227 (98.7%)	226 (98.7%)	453 (98.7%)
If present within past 12 months, ongoing	227 (98.7%)	226 (98.7%)	453 (98.7%)
No	99 (43.0%)	103 (45.0%)	202 (44.0%)
Yes	128 (55.7%)	123 (53.7%)	251 (54.7%)
Critical leg ischemia (rest pain or ischemic ulcer)	33 (14.3%)	31 (13.5%)	64 (13.9%)
If yes, critical leg ischemia present within past 12 months?	33 (14.3%)	31 (13.5%)	64 (13.9%)
No	3 (1.3%)	4 (1.7%)	7 (1.5%)
Yes	30 (13.0%)	27 (11.8%)	57 (12.4%)
If present within past 12 months, ongoing	30 (13.0%)	27 (11.8%)	57 (12.4%)
No	12 (5.2%)	10 (4.4%)	22 (4.8%)
Yes	18 (7.8%)	17 (7.4%)	35 (7.6%)
Ischemic lower extremity amputation below ankle	5 (2.2%)	3 (1.3%)	8 (1.7%)
If yes, affected limb			
BILATERAL	0	0	0
LEFT	1 (0.4%)	1 (0.4%)	2 (0.4%)
RIGHT	4 (1.7%)	2 (0.9%)	6 (1.3%)
Ischemic lower extremity amputation above ankle	0	2 (0.9%)	2 (0.4%)
If yes, affected limb			
BILATERAL	0	0	0
LEFT	0	1 (0.4%)	1 (0.2%)
RIGHT	0	1 (0.4%)	1 (0.2%)
Any non-ischemic amputation	0	2 (0.9%)	2 (0.4%)
If yes, type			
INFECTIOUS	0	0	0
OTHER	0	0	0
TRAUMA	0	2 (0.9%)	2 (0.4%)
Peripheral percutaneous transluminal angioplasty (prior to qualifying revascularization procedure)	92 (40.0%)	97 (42.4%)	189 (41.2%)
If yes, type			
missing	0	0	0
ATHERECTOMY	0	3 (1.3%)	3 (0.7%)
BALLOON (PTCA)	42 (18.3%)	51 (22.3%)	93 (20.3%)
BARE METAL STENT	45 (19.6%)	35 (15.3%)	80 (17.4%)
DRUG ELUTING STENT	4 (1.7%)	3 (1.3%)	7 (1.5%)
OTHER	1 (0.4%)	3 (1.3%)	4 (0.9%)
UNKNOWN STENT TYPE	0	2 (0.9%)	2 (0.4%)
If yes, affected limb	92 (40.0%)	97 (42.4%)	189 (41.2%)
missing	0	0	0
BILATERAL	9 (3.9%)	10 (4.4%)	19 (4.1%)
LEFT	42 (18.3%)	39 (17.0%)	81 (17.6%)
RIGHT	41 (17.8%)	48 (21.0%)	89 (19.4%)

	Rivaroxaban 2.5 mg bid + ASA 100 mg od N=230 (100%)	Rivaroxaban placebo bid + ASA 100 mg od N=229 (100%)	Total N=459 (100%)
Peripheral surgical bypass (prior to qualifying revascularization procedure)	20 (8.7%)	14 (6.1%)	34 (7.4%)
If yes, affected limb			
missing	0	0	0
BILATERAL	1 (0.4%)	0	1 (0.2%)
LEFT	8 (3.5%)	4 (1.7%)	12 (2.6%)
RIGHT	11 (4.8%)	10 (4.4%)	21 (4.6%)
Risk factors/comorbid conditions			
Diabetes mellitus	106 (46.1%)	109 (47.6%)	215 (46.8%)
If yes, type			
missing	0	0	0
TYPE I	0	0	0
TYPE II	106 (46.1%)	109 (47.6%)	215 (46.8%)
Family history of premature MI	8 (3.5%)	5 (2.2%)	13 (2.8%)
Chronic kidney disease	52 (22.6%)	33 (14.4%)	85 (18.5%)
If yes, GFR (ml/min/1.73m^2)			
missing	0	0	0
<30	1 (0.4%)	4 (1.7%)	5 (1.1%)
30 - 50	38 (16.5%)	19 (8.3%)	57 (12.4%)
>50-80	13 (5.7%)	10 (4.4%)	23 (5.0%)
>80	0	0	0
Gastrointestinal disease history			
Gastrointestinal bleeding history			
Gastrointestinal bleeding	8 (3.5%)	10 (4.4%)	18 (3.9%)
Gastrointestinal ulceration	15 (6.5%)	17 (7.4%)	32 (7.0%)
Gastrointestinal erosions	7 (3.0%)	4 (1.7%)	11 (2.4%)
Liver diseases	17 (7.4%)	8 (3.5%)	25 (5.4%)
Gastrointestinal bleeding and associated blood transfusion			
Bleeding requiring transfusion	6 (2.6%)	2 (0.9%)	8 (1.7%)
GI variceal bleeding	0	0	0
Prior emergent endoscopy procedures to control bleeding	1 (0.4%)	0	1 (0.2%)
Pulmonary history			
COPD	13 (5.7%)	17 (7.4%)	30 (6.5%)
Sleep apnea	2 (0.9%)	1 (0.4%)	3 (0.7%)

The ITT analysis set includes all randomized subjects, bid = twice daily, od = once daily, ASA = acetylsalicylic acid
STEMI = ST-elevation myocardial infarction, GFR = Glomerular Filtration Rate, MI = Myocardial infarction, PTCA = Percutaneous transluminal coronary angioplasty, IMA = internal mammary artery, NYHA = New York Heart Association, ICD = Implantable cardioverter-defibrillator, DES = Drug-Eluting Stent, BMS = Bare Metal Stent, GI = Gastro-intestinal.
Source: 5.3.5.1.2 17454_J_analysis/Table 14.1.3/1

表 2.7.3.7-8 病歴（試験 17454、血行再建術及びクロピドグレル使用に関する IxRS での層別、全体集団、ITT）

	Rivaroxaban 2.5 mg bid + ASA 100 mg od N=3286 (100%)			Rivaroxaban placebo bid + ASA 100 mg od N=3278 (100%)		
	Surgical	Endovascular with clopidogrel	Endovascular without clopidogrel	Surgical	Endovascular with clopidogrel	Endovascular without clopidogrel
	N=1133 (100%)	N=1539 (100%)	N=614 (100%)	N=1138 (100%)	N=1541 (100%)	N=599 (100%)
CAD	354 (31.2%)	534 (34.7%)	164 (26.7%)	326 (28.6%)	513 (33.3%)	176 (29.4%)
Angina pectoris	137 (12.1%)	181 (11.8%)	54 (8.8%)	123 (10.8%)	166 (10.8%)	59 (9.8%)
Myocardial infarction	133 (11.7%)	171 (11.1%)	61 (9.9%)	107 (9.4%)	168 (10.9%)	74 (12.4%)
Valvular heart disease	75 (6.6%)	94 (6.1%)	31 (5.0%)	76 (6.7%)	103 (6.7%)	33 (5.5%)
AFIB (prior history)	38 (3.4%)	40 (2.6%)	14 (2.3%)	30 (2.6%)	40 (2.6%)	18 (3.0%)
Atrial flutter (prior history)	4 (0.4%)	10 (0.6%)	1 (0.2%)	5 (0.4%)	3 (0.2%)	2 (0.3%)
PCI	107 (9.4%)	260 (16.9%)	75 (12.2%)	100 (8.8%)	236 (15.3%)	74 (12.4%)
CABG	80 (7.1%)	153 (9.9%)	55 (9.0%)	70 (6.2%)	133 (8.6%)	43 (7.2%)
CABG IMA graft	46 (4.1%)	95 (6.2%)	31 (5.0%)	40 (3.5%)	79 (5.1%)	22 (3.7%)
CABG ≥3 vessel bypass grafting	51 (4.5%)	93 (6.0%)	29 (4.7%)	45 (4.0%)	84 (5.5%)	23 (3.8%)
Heart failure	109 (9.6%)	119 (7.7%)	39 (6.4%)	110 (9.7%)	121 (7.9%)	41 (6.8%)
Pacemaker	10 (0.9%)	27 (1.8%)	4 (0.7%)	12 (1.1%)	35 (2.3%)	11 (1.8%)
Defibrillator	6 (0.5%)	10 (0.6%)	0	4 (0.4%)	20 (1.3%)	5 (0.8%)
Carotid artery stenosis ≥50%	85 (7.5%)	129 (8.4%)	36 (5.9%)	88 (7.7%)	135 (8.8%)	28 (4.7%)
Carotid endarterectomy	36 (3.2%)	39 (2.5%)	12 (2.0%)	32 (2.8%)	33 (2.1%)	12 (2.0%)
Percutaneous carotid intervention	7 (0.6%)	37 (2.4%)	4 (0.7%)	7 (0.6%)	31 (2.0%)	10 (1.7%)
Claudication within 12 months	1078 (95.1%)	1466 (95.3%)	575 (93.6%)	1099 (96.6%)	1458 (94.6%)	569 (95.0%)
Critical limb ischemia (rest pain/ischemic ulcer)	469 (41.4%)	366 (23.8%)	164 (26.7%)	442 (38.8%)	370 (24.0%)	157 (26.2%)
Critical limb ischemia categories						
Missing	1 (<0.1%)	0	0	1 (<0.1%)	0	0
No critical limb ischemia	663 (58.5%)	1173 (76.2%)	450 (73.3%)	695 (61.1%)	1171 (76.0%)	442 (73.8%)
Critical limb ischemia history	190 (16.8%)	151 (9.8%)	55 (9.0%)	188 (16.5%)	145 (9.4%)	54 (9.0%)
Critical limb ischemia ongoing	279 (24.6%)	215 (14.0%)	109 (17.8%)	254 (22.3%)	225 (14.6%)	103 (17.2%)
Ischemic lower extremity amputation below ankle	44 (3.9%)	68 (4.4%)	32 (5.2%)	40 (3.5%)	68 (4.4%)	34 (5.7%)

	Rivaroxaban 2.5 mg bid + ASA 100 mg od N=3286 (100%)			Rivaroxaban placebo bid + ASA 100 mg od N=3278 (100%)		
	Surgical	Endovascular with clopidogrel	Endovascular without clopidogrel	Surgical	Endovascular with clopidogrel	Endovascular without clopidogrel
	N=1133 (100%)	N=1539 (100%)	N=614 (100%)	N=1138 (100%)	N=1541 (100%)	N=599 (100%)
Ischemic lower extremity amputation above ankle	11 (1.0%)	21 (1.4%)	4 (0.7%)	14 (1.2%)	11 (0.7%)	4 (0.7%)
Any nonischemic amputation	13 (1.1%)	6 (0.4%)	6 (1.0%)	14 (1.2%)	14 (0.9%)	6 (1.0%)
Peripheral PTA [a]	197 (17.4%)	558 (36.3%)	198 (32.2%)	201 (17.7%)	581 (37.7%)	173 (28.9%)
Peripheral surgical bypass [a]	197 (17.4%)	103 (6.7%)	43 (7.0%)	182 (16.0%)	93 (6.0%)	44 (7.3%)
Diabetes mellitus	370 (32.7%)	683 (44.4%)	260 (42.3%)	339 (29.8%)	718 (46.6%)	259 (43.2%)
Family history of premature MI	80 (7.1%)	147 (9.6%)	38 (6.2%)	74 (6.5%)	119 (7.7%)	46 (7.7%)
Chronic kidney disease	51 (4.5%)	191 (12.4%)	75 (12.2%)	48 (4.2%)	179 (11.6%)	62 (10.4%)
GI bleeding	18 (1.6%)	33 (2.1%)	7 (1.1%)	14 (1.2%)	28 (1.8%)	7 (1.2%)
GI ulceration	48 (4.2%)	64 (4.2%)	23 (3.7%)	56 (4.9%)	61 (4.0%)	20 (3.3%)
GI erosion	14 (1.2%)	24 (1.6%)	6 (1.0%)	19 (1.7%)	14 (0.9%)	10 (1.7%)
Liver disease	38 (3.4%)	41 (2.7%)	19 (3.1%)	30 (2.6%)	42 (2.7%)	15 (2.5%)
GI bleeding requiring transfusion	8 (0.7%)	15 (1.0%)	6 (1.0%)	7 (0.6%)	12 (0.8%)	0
GI variceal bleed	0	1 (<0.1%)	0	1 (<0.1%)	0	0
Prior emergent endoscopy procedure to control bleeding	5 (0.4%)	8 (0.5%)	4 (0.7%)	5 (0.4%)	5 (0.3%)	1 (0.2%)
Chronic obstructive pulmonary disease	127 (11.2%)	169 (11.0%)	66 (10.7%)	148 (13.0%)	151 (9.8%)	51 (8.5%)
Sleep apnea	17 (1.5%)	61 (4.0%)	17 (2.8%)	15 (1.3%)	59 (3.8%)	21 (3.5%)

a：prior to qualifying revascularization procedure

AFIB = atrial fibrillation, ASA = acetylsalicylic acid, bid = twice daily, CABG = coronary artery bypass graft, CAD = coronary artery disease, Endovascular with clopidogrel = endovascular including hybrid with clopidogrel, Endovascular without clopidogrel = endovascular including hybrid without clopidogrel, GI = gastrointestinal, IMA = internal mammary artery, ITT = intention-to-treat, MI = myocardial infarction, od = once daily, PCI = percutaneous coronary intervention, PTA = percutaneous transluminal angioplasty

Source: 5.3.5.1.1 PH-40164/Table 14.1.3/2, Post-hoc Table 14.3.5.1.2/1,14.3.5.2.1/1.

表 2.7.3.7-9 外科的血行再建術の層におけるクロピドグレルの使用状況（試験 17454、IxRS での層別、日本人集団、ITT）

Clopidogrel use	Rivaroxaban 2.5 mg bid + ASA 100 mg od N=45 (100%)	Rivaroxaban placebo bid + ASA 100 mg od N=44 (100%)	Total N=89 (100%)
Clopidogrel use in relation to qualifying revascularization procedure, actual			
No	34 (75.6%)	33 (75.0%)	67 (75.3%)
Yes	11 (24.4%)	11 (25.0%)	22 (24.7%)
Unknown	0	0	0
If yes (For subjects with loading / maintenance dose information),			
Loading dose	9 (20.0%)	9 (20.5%)	18 (20.2%)
None	7 (15.6%)	8 (18.2%)	15 (16.9%)
150 mg	0	0	0
300 mg	0	0	0
600 mg	0	0	0
>600 mg	0	0	0
Other	2 (4.4%)	1 (2.3%)	3 (3.4%)
Maintenance dose	9 (20.0%)	9 (20.5%)	18 (20.2%)
75 mg	9 (20.0%)	9 (20.5%)	18 (20.2%)
150 mg	0	0	0
300 mg	0	0	0
Clopidogrel use continued after randomization			
No	38 (84.4%)	37 (84.1%)	75 (84.3%)
Yes	7 (15.6%)	7 (15.9%)	14 (15.7%)
Unknown	0	0	0
Duration of clopidogrel use after qualifying revascularization procedure (days)			
n	11	11	22
Nmiss	34	33	67
Mean	18.6	20.2	19.4
SD	13.6	11.4	12.3
Min	2	3	2
Q1	6.0	9.0	9.0
Median	22.0	26.0	23.5
Q3	28.0	30.0	29.0
Max	45	33	45

Clopidogrel use	Rivaroxaban 2.5 mg bid + ASA 100 mg od N=45 (100%)	Rivaroxaban placebo bid + ASA 100 mg od N=44 (100%)	Total N=89 (100%)
Duration of clopidogrel use after qualifying revascularization procedure (days)			
Clopidogrel related to index revascularization not continued	0	0	0
<=30	10 (22.2%)	9 (20.5%)	19 (21.3%)
>30-60	1 (2.2%)	2 (4.5%)	3 (3.4%)
>60-90	0	0	0
>90-180	0	0	0
>180	0	0	0
Clopidogrel use after qualifying revascularization procedure without drug coated device	0	2 (4.5%)	2 (2.2%)
Clopidogrel related to index revascularization not continued	0	0	0
<=30 days	0	0	0
>30-60 days	0	2 (4.5%)	2 (2.2%)
>60 days	0	0	0
Clopidogrel use after qualifying revascularization procedure with drug coated device	0	0	0
Clopidogrel related to index revascularization not continued	0	0	0
<=30 days	0	0	0
>30-60 days	0	0	0
>60 days	0	0	0

The ITT analysis set includes all randomized subjects.

bid = twice daily, od = once daily, ASA = acetylsalicylic acid

Subjects with clopidogrel use continued after randomization considers all subjects with clopidogrel dosing episodes including the day of randomization until 2 days after randomization and clopidogrel episode did not end on day of randomization

Clopidogrel use in relation to qualifying revascularization procedure, actual considers all subjects with clopidogrel dosing episodes including the day of revascularization until 2 days after and clopidogrel dosing episodes did not end on day of revascularization. Missing clopidogrel duration for subjects with prior stop, use more than 2 days after index revascularization or unknown start/end dates.

If subjects received multiple revascularization procedures, i.e. with drug coated device and without drug coated device, subjects are counted in both groups.

Source: 5.3.5.1.2 17454_J_analysis/Table 14.1.4/2

表 2.7.3.7-10 血管内血行再建術でクロピドグレル使用ありの層におけるクロピドグレルの使用状況（試験 17454、IxRS での層別、日本人集団、ITT）

Clopidogrel use	Rivaroxaban 2.5 mg bid + ASA 100 mg od N=110 (100%)	Rivaroxaban placebo bid + ASA 100 mg od N=110 (100%)	Total N=220 (100%)
Clopidogrel use in relation to qualifying revascularization procedure, actual			
No	4 (3.6%)	4 (3.6%)	8 (3.6%)
Yes	106 (96.4%)	105 (95.5%)	211 (95.9%)
Unknown	0	1 (0.9%)	1 (0.5%)
If yes (For subjects with loading / maintenance dose information),			
Loading dose	103 (93.6%)	104 (94.5%)	207 (94.1%)
None	82 (74.5%)	82 (74.5%)	164 (74.5%)
150 mg	1 (0.9%)	1 (0.9%)	2 (0.9%)
300 mg	4 (3.6%)	4 (3.6%)	8 (3.6%)
600 mg	0	0	0
>600 mg	0	0	0
Other	16 (14.5%)	17 (15.5%)	33 (15.0%)
Maintenance dose	101 (91.8%)	103 (93.6%)	204 (92.7%)
75 mg	101 (91.8%)	102 (92.7%)	203 (92.3%)
150 mg	0	0	0
300 mg	0	1 (0.9%)	1 (0.5%)
Clopidogrel use continued after randomization			
No	4 (3.6%)	5 (4.5%)	9 (4.1%)
Yes	105 (95.5%)	104 (94.5%)	209 (95.0%)
Unknown	1 (0.9%)	1 (0.9%)	2 (0.9%)
Duration of clopidogrel use after qualifying revascularization procedure (days)			
n	104	103	207
Nmiss	6	7	13
Mean	80.5	66.9	73.7
SD	113.2	88.8	101.8
Min	1	2	1
Q1	29.0	28.0	28.0
Median	31.0	30.0	30.0
Q3	96.0	69.0	85.0
Max	766	664	766

Clopidogrel use	Rivaroxaban 2.5 mg bid + ASA 100 mg od N=110 (100%)	Rivaroxaban placebo bid + ASA 100 mg od N=110 (100%)	Total N=220 (100%)
Duration of clopidogrel use after qualifying revascularization procedure (days)			
Clopidogrel related to index revascularization not continued	2 (1.8%)	2 (1.8%)	4 (1.8%)
<=30	51 (46.4%)	53 (48.2%)	104 (47.3%)
>30-60	21 (19.1%)	23 (20.9%)	44 (20.0%)
>60-90	5 (4.5%)	5 (4.5%)	10 (4.5%)
>90-180	17 (15.5%)	12 (10.9%)	29 (13.2%)
>180	10 (9.1%)	10 (9.1%)	20 (9.1%)
Clopidogrel use after qualifying revascularization procedure without drug coated device	102 (92.7%)	101 (91.8%)	203 (92.3%)
Clopidogrel related to index revascularization not continued	1 (0.9%)	2 (1.8%)	3 (1.4%)
<=30 days	51 (46.4%)	53 (48.2%)	104 (47.3%)
>30-60 days	19 (17.3%)	23 (20.9%)	42 (19.1%)
>60 days	31 (28.2%)	23 (20.9%)	54 (24.5%)
Clopidogrel use after qualifying revascularization procedure with drug coated device	10 (9.1%)	11 (10.0%)	21 (9.5%)
Clopidogrel related to index revascularization not continued	1 (0.9%)	0	1 (0.5%)
<=30 days	0	3 (2.7%)	3 (1.4%)
>30-60 days	8 (7.3%)	4 (3.6%)	12 (5.5%)
>60 days	1 (0.9%)	4 (3.6%)	5 (2.3%)

The ITT analysis set includes all randomized subjects.

bid = twice daily, od = once daily, ASA = acetylsalicylic acid

Subjects with clopidogrel use continued after randomization considers all subjects with clopidogrel dosing episodes including the day of randomization until 2 days after randomization and clopidogrel episode did not end on day of randomization

Clopidogrel use in relation to qualifying revascularization procedure, actual considers all subjects with clopidogrel dosing episodes including the day of revascularization until 2 days after and clopidogrel dosing episodes did not end on day of revascularization. Missing clopidogrel duration for subjects with prior stop, use more than 2 days after index revascularization or unknown start/end dates.

f subjects received multiple revascularization procedures, i.e. with drug coated device and without drug coated device, subjects are counted in both groups.

Source: 5.3.5.1.2 17454_J_analysis/Table 14.1.4/2

表 2.7.3.7-11 血管内血行再建術でクロピドグレル使用なしの層におけるクロピドグレルの使用状況（試験 17454、IxRS での層別、日本人集団、ITT）

Clopidogrel use	Rivaroxaban 2.5 mg bid + ASA 100 mg od N=75 (100%)	Rivaroxaban placebo bid + ASA 100 mg od N=75 (100%)	Total N=150 (100%)
Clopidogrel use in relation to qualifying revascularization procedure, actual			
No	60 (80.0%)	60 (80.0%)	120 (80.0%)
Yes	15 (20.0%)	15 (20.0%)	30 (20.0%)
Unknown	0	0	0
If yes (For subjects with loading / maintenance dose information),			
Loading dose	11 (14.7%)	9 (12.0%)	20 (13.3%)
None	10 (13.3%)	7 (9.3%)	17 (11.3%)
150 mg	0	0	0
300 mg	0	0	0
600 mg	0	0	0
>600 mg	0	0	0
Other	1 (1.3%)	2 (2.7%)	3 (2.0%)
Maintenance dose	11 (14.7%)	9 (12.0%)	20 (13.3%)
75 mg	11 (14.7%)	9 (12.0%)	20 (13.3%)
150 mg	0	0	0
300 mg	0	0	0
Clopidogrel use continued after randomization			
No	72 (96.0%)	72 (96.0%)	144 (96.0%)
Yes	3 (4.0%)	3 (4.0%)	6 (4.0%)
Unknown	0	0	0
Duration of clopidogrel use after qualifying revascularization procedure (days)			
n	15	15	30
Nmiss	60	60	120
Mean	19.1	10.5	14.8
SD	47.5	10.4	34.0
Min	1	1	1
Q1	4.0	3.0	4.0
Median	6.0	7.0	6.0
Q3	7.0	10.0	9.0
Max	189	30	189

Clopidogrel use	Rivaroxaban 2.5 mg bid + ASA 100 mg od N=75 (100%)	Rivaroxaban placebo bid + ASA 100 mg od N=75 (100%)	Total N=150 (100%)
Duration of clopidogrel use after qualifying revascularization procedure (days)			
Clopidogrel related to index revascularization not continued	0	0	0
<=30	14 (18.7%)	15 (20.0%)	29 (19.3%)
>30-60	0	0	0
>60-90	0	0	0
>90-180	0	0	0
>180	1 (1.3%)	0	1 (0.7%)
Clopidogrel use after qualifying revascularization procedure without drug coated device	15 (20.0%)	15 (20.0%)	30 (20.0%)
Clopidogrel related to index revascularization not continued	0	0	0
<=30 days	14 (18.7%)	15 (20.0%)	29 (19.3%)
>30-60 days	0	0	0
>60 days	1 (1.3%)	0	1 (0.7%)
Clopidogrel use after qualifying revascularization procedure with drug coated device	0	0	0
Clopidogrel related to index revascularization not continued	0	0	0
<=30 days	0	0	0
>30-60 days	0	0	0
>60 days	0	0	0

The ITT analysis set includes all randomized subjects.
bid = twice daily, od = once daily, ASA = acetylsalicylic acid
Subjects with clopidogrel use continued after randomization considers all subjects with clopidogrel dosing episodes including the day of randomization until 2 days after randomization and clopidogrel episode did not end on day of randomization
Clopidogrel use in relation to qualifying revascularization procedure, actual considers all subjects with clopidogrel dosing episodes including the day of revascularization until 2 days after and clopidogrel dosing episodes did not end on day of revascularization. Missing clopidogrel duration for subjects with prior stop, use more than 2 days after index revascularization or unknown start/end dates.
If subjects received multiple revascularization procedures, i.e. with drug coated device and without drug coated device, subjects are counted in both groups.
Source: 5.3.5.1.2 17454_J_analysis/Table 14.1.4/2

表 2.7.3.7-12 有効性副次評価項目の感度分析：主解析（ITT、ECOD まで）と On-treatment 解析（SAF）の結果の比較（試験 17454、全体集団、ICAC 判定 c）

	Primary Analysis until the ECOD (ITT analysis set) a Rivaroxaban 2.5 mg bid + ASA 100 mg od vs Rivaroxaban placebo bid + ASA 100 mg od		**On-treatment Sensitivity Analysis (SAF) b Rivaroxaban 2.5 mg bid + ASA 100 mg od vs Rivaroxaban placebo bid + ASA 100 mg od**	
Outcome Components c	HR (95% CI)	P-value (1-sided/ 2-sided)	HR (95% CI)	P-value (2-sided)
MI, ischemic stroke, CHD death, ALI, and major amputation	0.80 (0.71, 0.91)	**0.0004/** 0.0008	0.73 (0.63, 0.84)	<0.0001
CHD death	1.09 (0.80, 1.48)	0.7082/ 0.5836	0.90 (0.60, 1.34)	0.5921
Unplanned index limb revascularization for recurrent limb ischemia	0.88 (0.79, 0.99)	**0.0140/** 0.0280	0.89 (0.79, 1.00)	0.0528
Hospitalization for a coronary or peripheral cause (either lower limb) of a thrombotic nature	0.72 (0.62, 0.85)	**<0.0001**/ <0.0001	0.66 (0.55, 0.78)	<0.0001
MI, ischemic stroke, all-cause mortality, ALI, and major amputation of a vascular etiology	0.89 (0.79, 0.99)	**0.0145**/ 0.0289	0.74 (0.65, 0.85)	<0.0001
MI, all-cause stroke, CV death, ALI, and major amputation of a vascular etiology	0.86 (0.76, 0.96)	**0.0051**/ 0.0103	0.75 (0.66, 0.87)	<0.0001
All-cause stroke	0.94 (0.70, 1.28)	0.3501/ 0.7001	0.86 (0.60, 1.23)	0.4133
All-cause mortality	1.08 (0.92, 1.27)	0.8322/ 0.3356	0.84 (0.64, 1.09)	0.1843
CV death	1.14 (0.93, 1.40)	0.9015/ 0.1971	0.92 (0.68, 1.25)	0.6119
Non-CV death	0.99 (0.77, 1.27)	0.4753/ 0.9507	0.63 (0.38, 1.07)	0.0832
Venous thromboembolic events	0.61 (0.37, 1.00)	0.0235/ 0.0469	0.30 (0.14, 0.62)	0.0006

a: The ITT data scope includes outcome events observed from randomization until the efficacy cut-off date.

b: The on-treatment data scope includes outcome events from randomization until 2 days after permanent stop of study drug (rivaroxaban or placebo).

c: “Unplanned index limb revascularization for recurrent limb ischemia（あらかじめ計画されていなかったインデックス肢に対する血行再建術）”及び“venous thromboembolic events（VTE）”は治験責任（分担）医師の判定に基づく。

Efficacy cut-off date = 08 SEP 2019.

MI, stroke, mortality, ALI and major amputation of a vascular etiology and events leading to hospitalization are adjudicated; index limb revascularization and venous thromboembolic events are reported by investigator only.

Index limb revascularization is defined as subsequent index leg revascularization that was not planned or considered as part of the initial treatment plan at the time of randomization.

HR (95% CI) is based on the Cox proportional hazards model stratified by type of procedure and clopidogrel use, per IxRS assignment, with treatment as the only covariate. P-value is based on the log rank test stratified by type of procedure and clopidogrel use per IxRS assignment with treatment as a factor.

ALI = acute limb ischemia, ASA = acetylsalicylic acid, bid = twice daily, CI = confidence interval, CHD = coronary heart disease, CV = cardiovascular, CV death = cardiovascular death and death of unknown cause, ECOD = efficacy cut-off date, ITT = intention-to-treat, MI = myocardial infarction, od = once daily, SAF = safety analysis set.

Source: 5.3.5.1.1 PH-40164/Table 14.2.2/1,14.2.6/56

表 2.7.3.7-13 ECOD までに発現した全死亡、心血管死及び非心血管死（試験 17454、無作為割付け時のクロピドグレル使用の有無別、全体集団、ITT、ICAC 判定）

	Rivaroxaban 2.5 mg bid + ASA 100 mg od		Rivaroxaban placebo bid + ASA 100 mg od		Rivaroxaban 2.5 mg bid + ASA 100 mg od vs Rivaroxaban placebo bid + ASA 100 mg od	
	n (%)	n/100p-yrs (95% CI)	n (%)	n/100p-yrs (95% CI)	HR (95% CI)	P-value (2-sided)
Clopidogrel use at the time of randomization: No						
All-cause mortality	174/1621 (10.7%)	4.37 (3.75; 5.07)	162/1613 (10.0%)	4.09 (3.48; 4.77)	1.07 (0.86, 1.32)	0.5414
CV death	104/1621 (6.4%)	2.61 (2.14; 3.17)	98/1613 (6.1%)	2.47 (2.01; 3.01)	1.06 (0.80, 1.39)	0.6930
Non-CV death	70/1621 (4.3%)	1.76 (1.37; 2.22)	64/1613 (4.0%)	1.61 (1.24; 2.06)	1.09 (0.77, 1.53)	0.6293
Clopidogrel use at the time of randomization: Yes						
All-cause mortality	147/1658 (8.9%)	3.61 (3.05; 4.24)	134/1655 (8.1%)	3.28 (2.75; 3.88)	1.10 (0.87, 1.39)	0.4278
CV death	95/1658 (5.7%)	2.33 (1.89; 2.85)	75/1655 (4.5%)	1.83 (1.44; 2.30)	1.27 (0.94, 1.72)	0.1180
Non-CV death	52/1658 (3.1%)	1.28 (0.95; 1.68)	59/1655 (3.6%)	1.44 (1.10; 1.86)	0.88 (0.61, 1.28)	0.5014

Table displays outcome events as adjudicated by Independent Clinical Adjudication Committee (ICAC).

The ITT analysis set includes all randomized subjects. The overall study duration data scope includes outcome events observed from randomization until the last contact/visit. CV death includes death of unknown cause.

Only the first occurrence of the outcome event under analysis within the data scope from a subject is considered. HR (95% CI) is based on the Cox proportional hazards model stratified by type of procedure and clopidogrel use (per IxRS) with treatment as the only covariate. P-value is based on the log rank test stratified by type of procedure and clopidogrel use per IxRS assignment with treatment as a factor.

ASA = acetylsalicylic acid, bid = twice daily, CI = confidence interval, CV = cardiovascular, HR = hazard ratio, ITT = intention-to-treat, od = once daily, n = number of subjects with events, % = 100 * n/N, n/100p-yrs = ratio of number of subjects with incident events / cumulative at-risk time.

Source: 5.3.5.1.1 PH-40164/Post-hoc Table 14.3.6.3.2/1

表 2.7.3.7-14 全死亡の内訳（試験 17454、全体集団、ICAC 判定）

	Until ECOD (ITT analysis set)		On-treatment (SAF)		≥3 days after last dose (SAF)*		3 to 30 days after last dose (SAF)		>30 days after last dose (SAF)*	
	Riva + ASA N=3286 (100%)	Plac + ASA N=3278 (100%)	Riva + ASA N=3256 (100%)	Plac + ASA N=3248 (100%)	Riva + ASA N=3256 (100%)	Plac + ASA N=3248 (100%)	Riva + ASA N=3256 (100%)	Plac + ASA N=3248 (100%)	Riva + ASA N=3256 (100%)	Plac + ASA N=3248 (100%)
Any death	**321 (9.8%)**	**297 (9.1%)**	**102 (3.1%)**	**124 (3.8%)**	**225 (6.9%)**	**180 (5.5%)**	**68 (2.1%)**	**50 (1.5%)**	**157 (4.8%)**	**130 (4.0%)**
CV death excluding unknown death	**137 (4.2%)**	**120 (3.7%)**	**52 (1.6%)**	**61 (1.9%)**	**86 (2.6%)**	**64 (2.0%)**	**32 (1.0%)**	**25 (0.8%)**	**54 (1.7%)**	**39 (1.2%)**
CHD death	85 (2.6%)	78 (2.4%)	44 (1.4%)	50 (1.5%)	40 (1.2%)	32 (1.0%)	13 (0.4%)	9 (0.3%)	27 (0.8%)	23 (0.7%)
Sudden cardiac arrest	55 (1.7%)	50 (1.5%)	37 (1.1%)	37 (1.1%)	18 (0.6%)	15 (0.5%)	5 (0.2%)	3 (<0.1%)	13 (0.4%)	12 (0.4%)
Acute MI	16 (0.5%)	21 (0.6%)	4 (0.1%)	12 (0.4%)	12 (0.4%)	10 (0.3%)	2 (<0.1%)	4 (0.1%)	10 (0.3%)	6 (0.2%)
CV cause of death [a]	11 (0.3%)	6 (0.2%)	2 (<0.1%)	1 (<0.1%)	9 (0.3%)	5 (0.2%)	6 (0.2%)	2 (<0.1%)	3 (<0.1%)	3 (<0.1%)
Complications from a coronary revascularization procedure	3 (<0.1%)	1 (<0.1%)	1 (<0.1%)	0	1 (<0.1%)	2 (<0.1%)	0	0	1 (<0.1%)	2 (<0.1%)
Non-CHD death	52 (1.6%)	42 (1.3%)	8 (0.2%)	11 (0.3%)	46 (1.4%)	32 (1.0%)	19 (0.6%)	16 (0.5%)	27 (0.8%)	16 (0.5%)
Cardiogenic shock (not related to acute MI)	7 (0.2%)	4 (0.1%)	1 (<0.1%)	1 (<0.1%)	7 (0.2%)	3 (<0.1%)	2 (<0.1%)	3 (<0.1%)	5 (0.2%)	0
Chronic heart failure	10 (0.3%)	5 (0.2%)	1 (<0.1%)	1 (<0.1%)	9 (0.3%)	4 (0.1%)	3 (<0.1%)	0	6 (0.2%)	4 (0.1%)
Immediate complications from a non-coronary CV procedure	8 (0.2%)	3 (<0.1%)	3 (<0.1%)	1 (<0.1%)	5 (0.2%)	2 (<0.1%)	3 (<0.1%)	1 (<0.1%)	2 (<0.1%)	1 (<0.1%)
Mesenteric ischemia	2 (<0.1%)	5 (0.2%)	0	1 (<0.1%)	2 (<0.1%)	4 (0.1%)	1 (<0.1%)	1 (<0.1%)	1 (<0.1%)	3 (<0.1%)
Other thromboembolic event	1 (<0.1%)	0	0	0	1 (<0.1%)	0	0	0	1 (<0.1%)	0
Peripheral arterial disease	12 (0.4%)	10 (0.3%)	0	3 (<0.1%)	13 (0.4%)	7 (0.2%)	6 (0.2%)	3 (<0.1%)	7 (0.2%)	4 (0.1%)
PE	0	6 (0.2%)	0	3 (<0.1%)	0	3 (<0.1%)	0	0	0	3 (<0.1%)
Stroke (Ischemic or unknown types only)	12 (0.4%)	9 (0.3%)	3 (<0.1%)	1 (<0.1%)	9 (0.3%)	9 (0.3%)	4 (0.1%)	8 (0.2%)	5 (0.2%)	1 (<0.1%)
Death of unknown cause	**62 (1.9%)**	**54 (1.6%)**	**27 (0.8%)**	**26 (0.8%)**	**36 (1.1%)**	**27 (0.8%)**	**6 (0.2%)**	**1 (<0.1%)**	**30 (0.9%)**	**26 (0.8%)**
Non-CV death	**122 (3.7%)**	**123 (3.8%)**	**23 (0.7%)**	**37 (1.1%)**	**103 (3.2%)**	**89 (2.7%)**	**30 (0.9%)**	**24 (0.7%)**	**73 (2.2%)**	**65 (2.0%)**

[a] within 30 days of an acute MI, related to the immediate consequences of the MI (e.g., heart failure, arrhythmia)

* until last contact

Table displays outcome events as adjudicated by Independent Clinical Adjudication Committee (ICAC).

ASA = acetylsalicylic acid, bid = twice daily, CHD = coronary heart disease, CV death = cardiovascular death and death of unknown cause, ECOD = efficacy cut-off date, ITT = intention to treat, N = total number of subjects, % = 100 * n / N, MI = myocardial infarction, od = once daily, PE = pulmonary embolism, Plac + ASA = rivaroxaban placebo bid + ASA 100 mg od, Riva + ASA = rivaroxaban 2.5 mg bid + ASA 100 mg od, SAF = safety analysis set

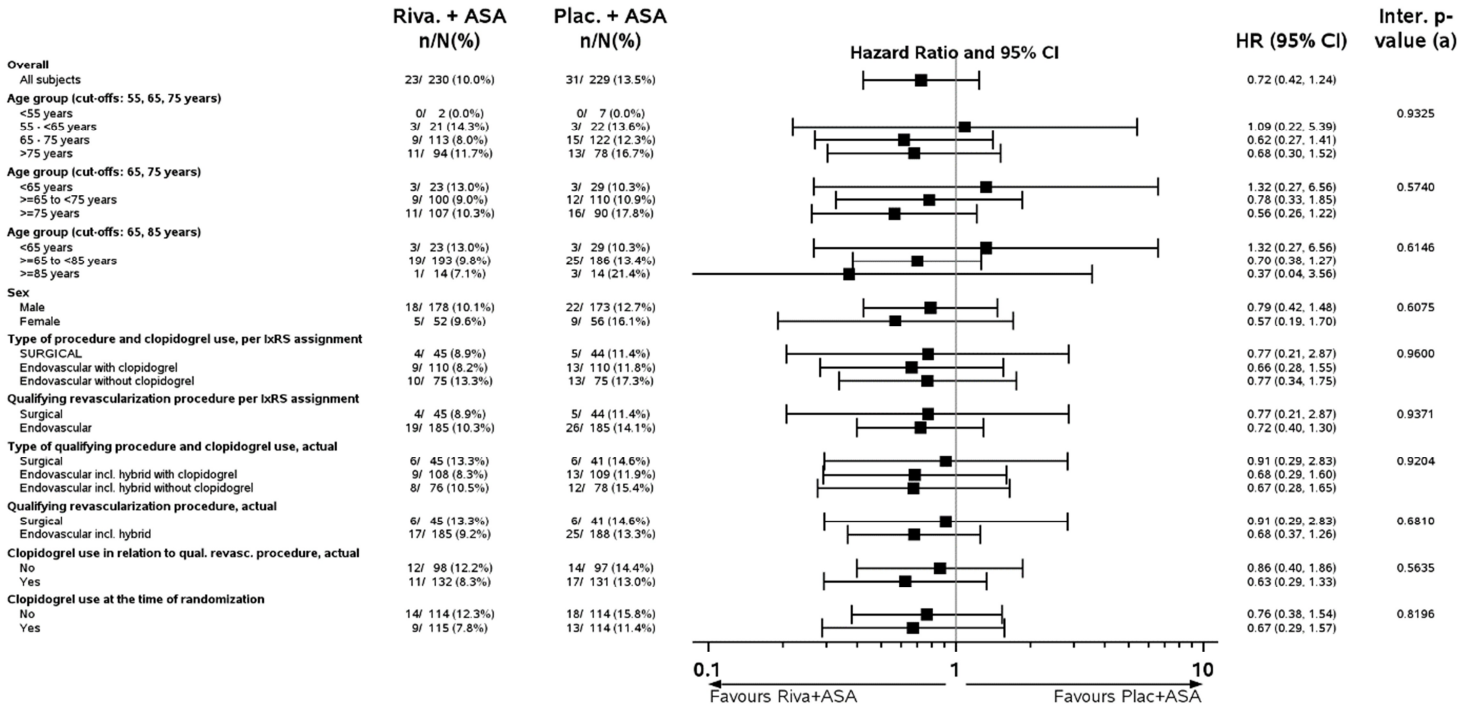
The safety analysis set includes all randomized subjects who received at least one dose of study drug (rivaroxaban or rivaroxaban placebo).

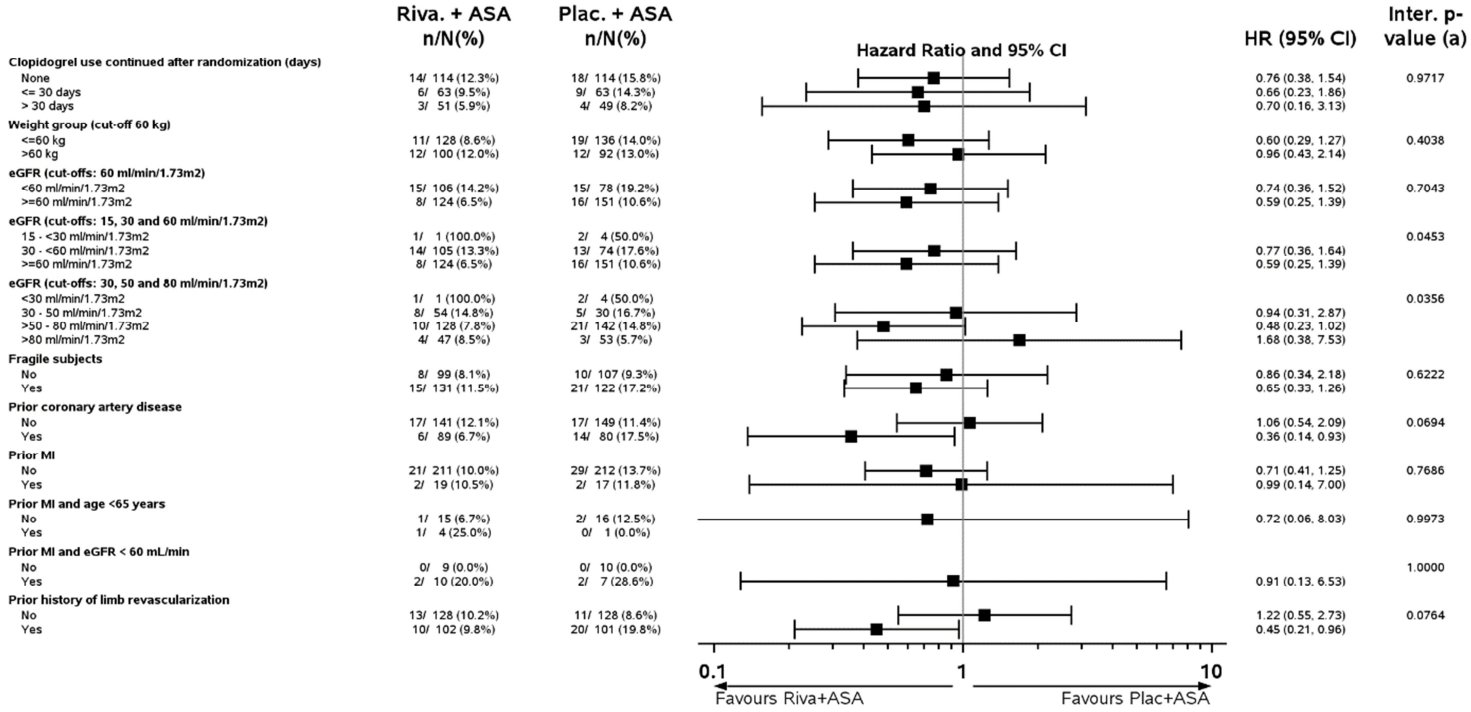
The on-treatment data scope includes outcome events from randomization until 2 days after permanent stop of study drug (rivaroxaban or rivaroxaban placebo).

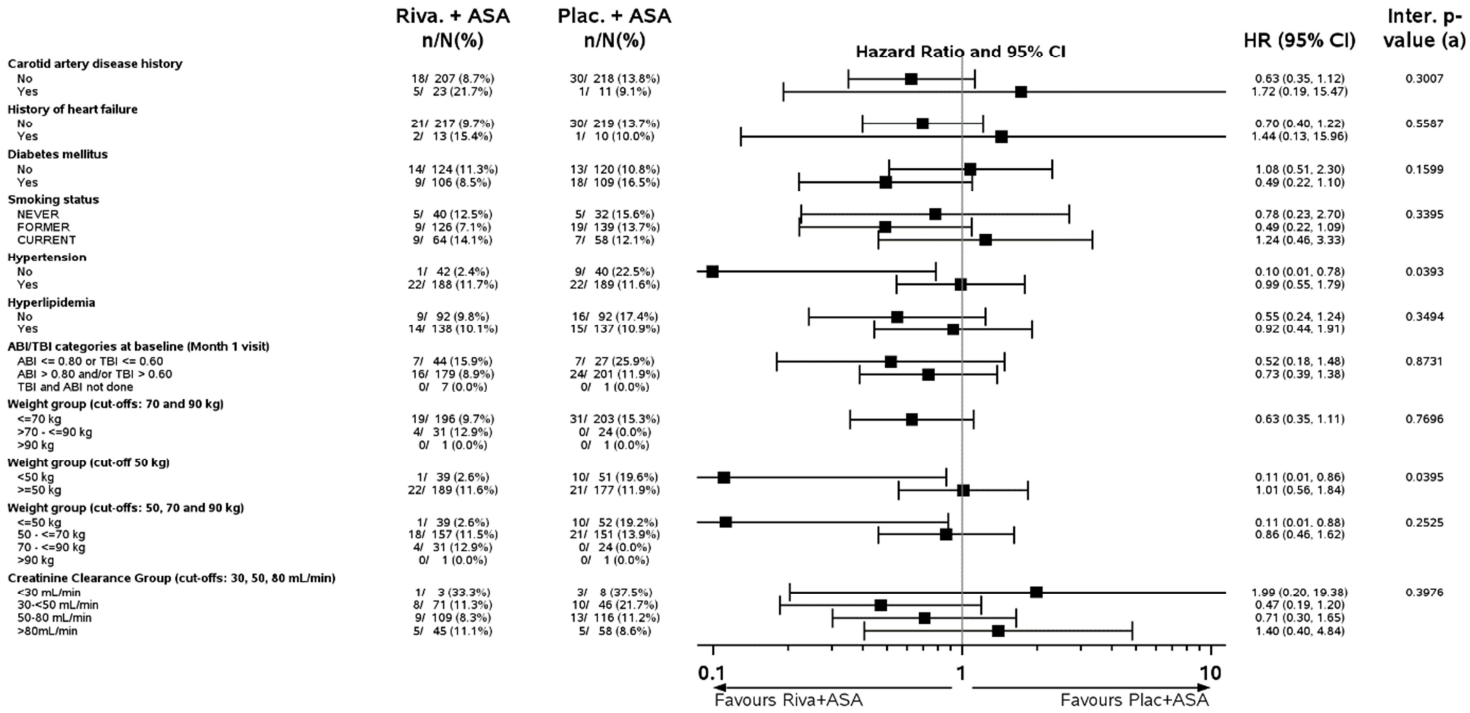
Source: 5.3.5.1.1 PH-40164/Table 14.3.1.1/25, 14.3.1.1/26, Post-hoc Table 14.3.6.3.1/19, 14.3.6.3.1/22, 14.3.6.3.1/25

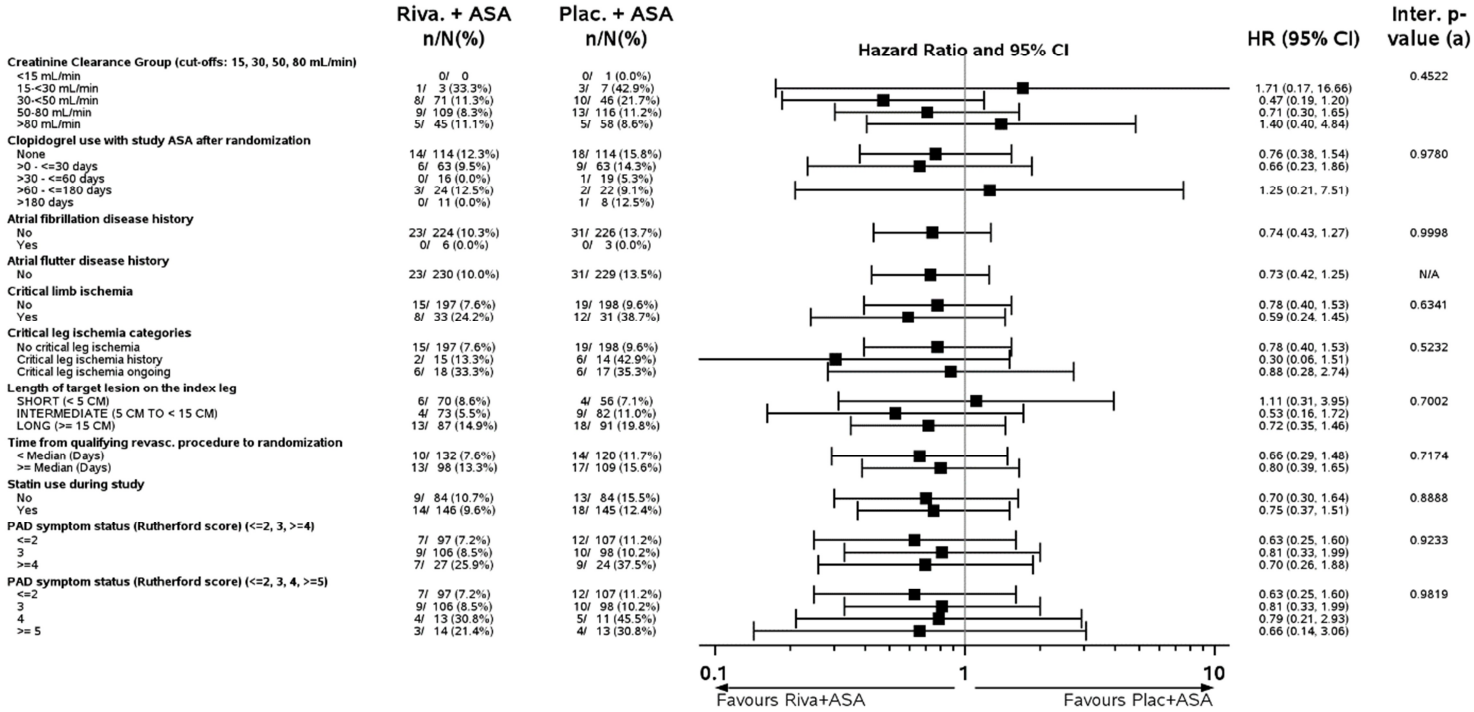
付図

図 2.7.3.7-1 有効性主要評価項目の Forest プロット（試験 17454、日本人集団、ITT、ECOD まで、ICAC 判定）




Riva. + ASA n/N(%)
Plac. + ASA n/N(%)
Hazard Ratio and 95% CI
HR (95% CI)
Inter. p-value (a)
Clopidogrel use continued after randomization (days)
None 14/ 114 (12.3%) 18/ 114 (15.8%) 0.76 (0.38, 1.54) 0.9717
<= 30 days 6/ 63 (9.5%) 9/ 63 (14.3%) 0.66 (0.23, 1.86)
> 30 days 3/ 51 (5.9%) 4/ 49 (8.2%) 0.70 (0.16, 3.13)
Weight group (cut-off 60 kg)
<=60 kg 11/ 128 (8.6%) 19/ 136 (14.0%) 0.60 (0.29, 1.27) 0.4038
>60 kg 12/ 100 (12.0%) 12/ 92 (13.0%) 0.96 (0.43, 2.14)
eGFR (cut-offs: 60 ml/min/1.73m2)
<60 ml/min/1.73m2 15/ 106 (14.2%) 15/ 78 (19.2%) 0.74 (0.36, 1.52) 0.7043
>=60 ml/min/1.73m2 8/ 124 (6.5%) 16/ 151 (10.6%) 0.59 (0.25, 1.39)
eGFR (cut-offs: 15, 30 and 60 ml/min/1.73m2)
15 - <30 ml/min/1.73m2 1/ 1 (100.0%) 2/ 4 (50.0%) 0.0453
30 - <60 ml/min/1.73m2 14/ 105 (13.3%) 13/ 74 (17.6%) 0.77 (0.36, 1.64)
>=60 ml/min/1.73m2 8/ 124 (6.5%) 16/ 151 (10.6%) 0.59 (0.25, 1.39)
eGFR (cut-offs: 30, 50 and 80 ml/min/1.73m2)
<30 ml/min/1.73m2 1/ 1 (100.0%) 2/ 4 (50.0%) 0.0356
30 - 50 ml/min/1.73m2 8/ 54 (14.8%) 5/ 30 (16.7%) 0.94 (0.31, 2.87)
>50 - 80 ml/min/1.73m2 10/ 128 (7.8%) 21/ 142 (14.8%) 0.48 (0.23, 1.02)
>80 ml/min/1.73m2 4/ 47 (8.5%) 3/ 53 (5.7%) 1.68 (0.38, 7.53)
Fragile subjects
No 8/ 99 (8.1%) 10/ 107 (9.3%) 0.86 (0.34, 2.18) 0.6222
Yes 15/ 131 (11.5%) 21/ 122 (17.2%) 0.65 (0.33, 1.26)
Prior coronary artery disease
No 17/ 141 (12.1%) 17/ 149 (11.4%) 1.06 (0.54, 2.09) 0.0694
Yes 6/ 89 (6.7%) 14/ 80 (17.5%) 0.36 (0.14, 0.93)
Prior MI
No 21/ 211 (10.0%) 29/ 212 (13.7%) 0.71 (0.41, 1.25) 0.7686
Yes 2/ 19 (10.5%) 2/ 17 (11.8%) 0.99 (0.14, 7.00)
Prior MI and age <65 years
No 1/ 15 (6.7%) 2/ 16 (12.5%) 0.72 (0.06, 8.03) 0.9973
Yes 1/ 4 (25.0%) 0/ 1 (0.0%)
Prior MI and eGFR < 60 mL/min
No 0/ 9 (0.0%) 0/ 10 (0.0%) 1.0000
Yes 2/ 10 (20.0%) 2/ 7 (28.6%) 0.91 (0.13, 6.53)
Prior history of limb revascularization
No 13/ 128 (10.2%) 11/ 128 (8.6%) 1.22 (0.55, 2.73) 0.0764
Yes 10/ 102 (9.8%) 20/ 101 (19.8%) 0.45 (0.21, 0.96)
0.1
1
10
Favours Riva+ASA
Favours Plac+ASA


Riva. + ASA n/N(%)
Plac. + ASA n/N(%)
Hazard Ratio and 95% CI
HR (95% CI)
Inter. p-value (a)
Carotid artery disease history
No 18/ 207 (8.7%) 30/ 218 (13.8%) 0.63 (0.35, 1.12) 0.3007
Yes 5/ 23 (21.7%) 1/ 11 (9.1%) 1.72 (0.19, 15.47)
History of heart failure
No 21/ 217 (9.7%) 30/ 219 (13.7%) 0.70 (0.40, 1.22) 0.5567
Yes 2/ 13 (15.4%) 1/ 10 (10.0%) 1.44 (0.13, 15.96)
Diabetes mellitus
No 14/ 124 (11.3%) 13/ 120 (10.8%) 1.08 (0.51, 2.30) 0.1599
Yes 9/ 106 (8.5%) 18/ 109 (16.5%) 0.49 (0.22, 1.10)
Smoking status
NEVER 5/ 40 (12.5%) 5/ 32 (15.6%) 0.78 (0.23, 2.70) 0.3395
FORMER 9/ 126 (7.1%) 19/ 139 (13.7%) 0.49 (0.22, 1.09)
CURRENT 9/ 64 (14.1%) 7/ 58 (12.1%) 1.24 (0.46, 3.33)
Hypertension
No 1/ 42 (2.4%) 9/ 40 (22.5%) 0.10 (0.01, 0.78) 0.0393
Yes 22/ 188 (11.7%) 22/ 189 (11.6%) 0.99 (0.55, 1.79)
Hyperlipidemia
No 9/ 92 (9.8%) 16/ 92 (17.4%) 0.55 (0.24, 1.24) 0.3494
Yes 14/ 138 (10.1%) 15/ 137 (10.9%) 0.92 (0.44, 1.91)
ABI/TBI categories at baseline (Month 1 visit)
ABI <= 0.80 or TBI <= 0.60 7/ 44 (15.9%) 7/ 27 (25.9%) 0.52 (0.18, 1.48) 0.8731
ABI > 0.80 and/or TBI > 0.60 16/ 179 (8.9%) 24/ 201 (11.9%) 0.73 (0.39, 1.38)
TBI and ABI not done 0/ 7 (0.0%) 0/ 1 (0.0%)
Weight group (cut-offs: 70 and 90 kg)
<=70 kg 19/ 196 (9.7%) 31/ 203 (15.3%) 0.63 (0.35, 1.11) 0.7696
>70 - <=90 kg 4/ 31 (12.9%) 0/ 24 (0.0%)
>90 kg 0/ 1 (0.0%) 0/ 1 (0.0%)
Weight group (cut-off 50 kg)
<50 kg 1/ 39 (2.6%) 10/ 51 (19.6%) 0.11 (0.01, 0.86) 0.0395
>=50 kg 22/ 189 (11.6%) 21/ 177 (11.9%) 1.01 (0.56, 1.84)
Weight group (cut-offs: 50, 70 and 90 kg)
<=50 kg 1/ 39 (2.6%) 10/ 52 (19.2%) 0.11 (0.01, 0.88) 0.2525
50 - <=70 kg 18/ 157 (11.5%) 21/ 151 (13.9%) 0.86 (0.46, 1.62)
70 - <=90 kg 4/ 31 (12.9%) 0/ 24 (0.0%)
>90 kg 0/ 1 (0.0%) 0/ 1 (0.0%)
Creatinine Clearance Group (cut-offs: 30, 50, 80 mL/min)
<30 mL/min 1/ 3 (33.3%) 3/ 8 (37.5%) 1.99 (0.20, 19.38) 0.3976
30-<50 mL/min 8/ 71 (11.3%) 10/ 46 (21.7%) 0.47 (0.19, 1.20)
50-80 mL/min 9/ 109 (8.3%) 13/ 116 (11.2%) 0.71 (0.30, 1.65)
>80mL/min 5/ 45 (11.1%) 5/ 58 (8.6%) 1.40 (0.40, 4.84)
0.1
1
10
Favours Riva+ASA
Favours Plac+ASA


Riva. + ASA n/N(%)
Plac. + ASA n/N(%)
Hazard Ratio and 95% CI
HR (95% CI)
Inter. p-value (a)
Creatinine Clearance Group (cut-offs: 15, 30, 50, 80 mL/min)
<15 mL/min 0/ 0 0/ 1 (0.0%) 0.4522
15-<30 mL/min 1/ 3 (33.3%) 3/ 7 (42.9%) 1.71 (0.17, 16.66)
30-<50 mL/min 8/ 71 (11.3%) 10/ 46 (21.7%) 0.47 (0.19, 1.20)
50-80 mL/min 9/ 109 (8.3%) 13/ 116 (11.2%) 0.71 (0.30, 1.65)
>80 mL/min 5/ 45 (11.1%) 5/ 58 (8.6%) 1.40 (0.40, 4.84)
Clopidogrel use with study ASA after randomization
None 14/ 114 (12.3%) 18/ 114 (15.8%) 0.76 (0.38, 1.54) 0.9780
>0 - <=30 days 6/ 63 (9.5%) 9/ 63 (14.3%) 0.66 (0.23, 1.86)
>30 - <=60 days 0/ 16 (0.0%) 1/ 19 (5.3%)
>60 - <=180 days 3/ 24 (12.5%) 2/ 22 (9.1%) 1.25 (0.21, 7.51)
>180 days 0/ 11 (0.0%) 1/ 8 (12.5%)
Atrial fibrillation disease history
No 23/ 224 (10.3%) 31/ 226 (13.7%) 0.74 (0.43, 1.27) 0.9998
Yes 0/ 6 (0.0%) 0/ 3 (0.0%)
Atrial flutter disease history
No 23/ 230 (10.0%) 31/ 229 (13.5%) 0.73 (0.42, 1.25) N/A
Critical limb ischemia
No 15/ 197 (7.6%) 19/ 198 (9.6%) 0.78 (0.40, 1.53) 0.6341
Yes 8/ 33 (24.2%) 12/ 31 (38.7%) 0.59 (0.24, 1.45)
Critical leg ischemia categories
No critical leg ischemia 15/ 197 (7.6%) 19/ 198 (9.6%) 0.78 (0.40, 1.53) 0.5232
Critical leg ischemia history 2/ 15 (13.3%) 6/ 14 (42.9%) 0.30 (0.06, 1.51)
Critical leg ischemia ongoing 6/ 18 (33.3%) 6/ 17 (35.3%) 0.88 (0.28, 2.74)
Length of target lesion on the index leg
SHORT (< 5 CM) 6/ 70 (8.6%) 4/ 56 (7.1%) 1.11 (0.31, 3.95) 0.7002
INTERMEDIATE (5 CM TO < 15 CM) 4/ 73 (5.5%) 9/ 82 (11.0%) 0.53 (0.16, 1.72)
LONG (>= 15 CM) 13/ 87 (14.9%) 18/ 91 (19.8%) 0.72 (0.35, 1.46)
Time from qualifying revasc. procedure to randomization
< Median (Days) 10/ 132 (7.6%) 14/ 120 (11.7%) 0.66 (0.29, 1.48) 0.7174
>= Median (Days) 13/ 98 (13.3%) 17/ 109 (15.6%) 0.80 (0.39, 1.65)
Statin use during study
No 9/ 84 (10.7%) 13/ 84 (15.5%) 0.70 (0.30, 1.64) 0.8888
Yes 14/ 146 (9.6%) 18/ 145 (12.4%) 0.75 (0.37, 1.51)
PAD symptom status (Rutherford score) (<=2, 3, >=4)
<=2 7/ 97 (7.2%) 12/ 107 (11.2%) 0.63 (0.25, 1.60) 0.9233
3 9/ 106 (8.5%) 10/ 98 (10.2%) 0.81 (0.33, 1.99)
>=4 7/ 27 (25.9%) 9/ 24 (37.5%) 0.70 (0.26, 1.88)
PAD symptom status (Rutherford score) (<=2, 3, 4, >=5)
<=2 7/ 97 (7.2%) 12/ 107 (11.2%) 0.63 (0.25, 1.60) 0.9819
3 9/ 106 (8.5%) 10/ 98 (10.2%) 0.81 (0.33, 1.99)
4 4/ 13 (30.8%) 5/ 11 (45.5%) 0.79 (0.21, 2.93)
>= 5 3/ 14 (21.4%) 4/ 13 (30.8%) 0.66 (0.14, 3.06)
0.1
1
10
Favours Riva+ASA
Favours Plac+ASA

Region: Japan

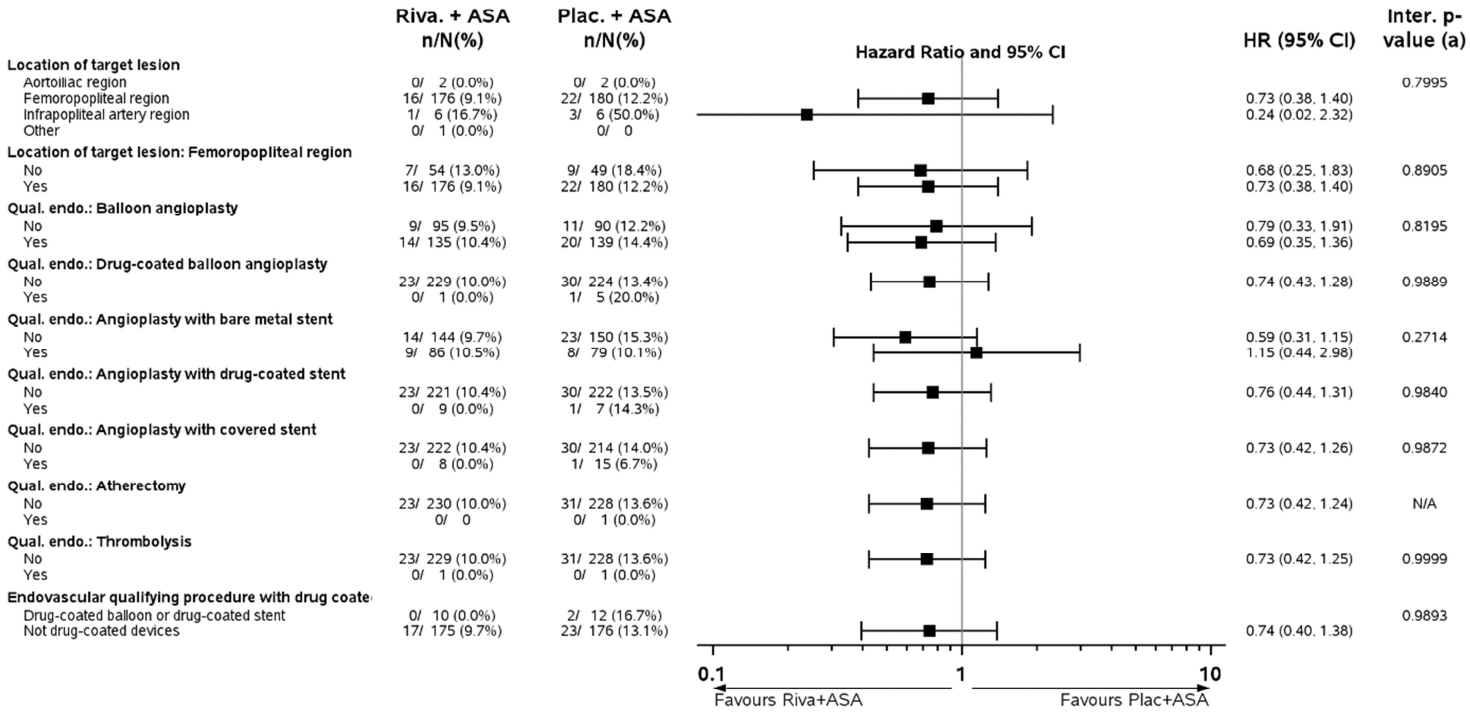
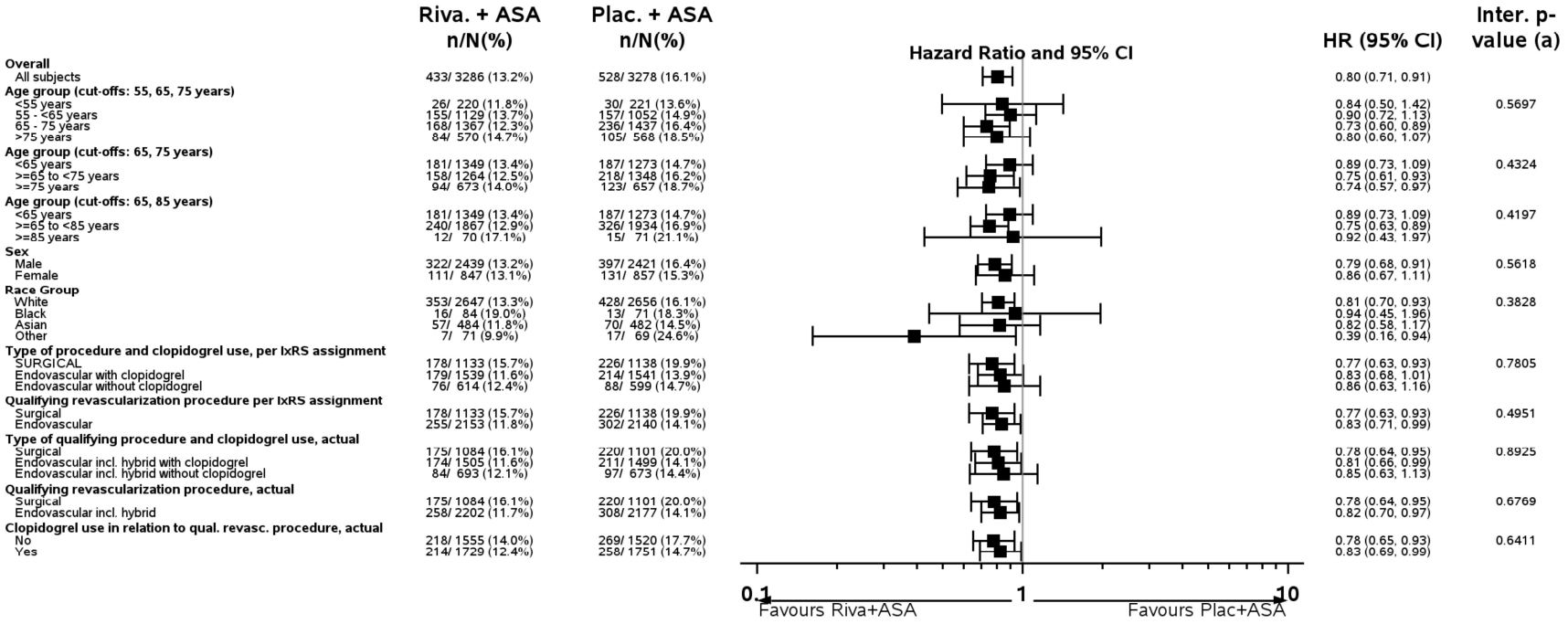
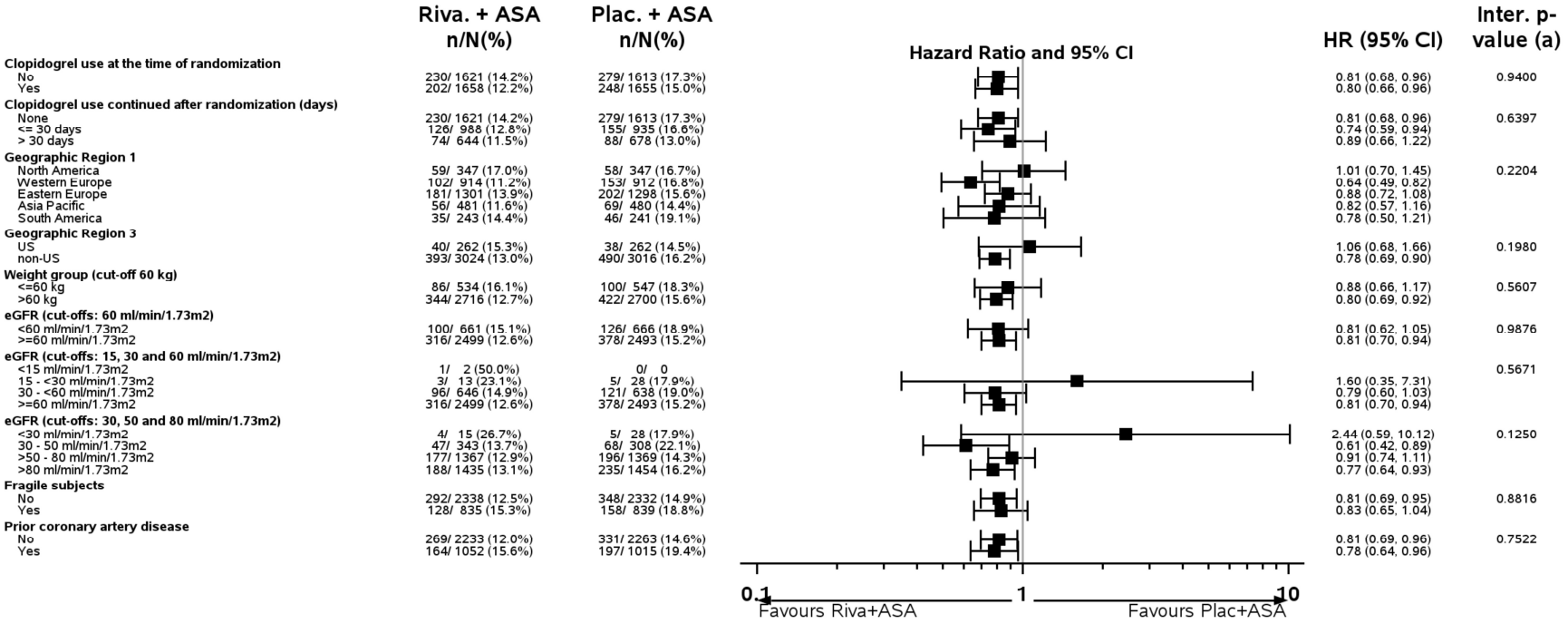


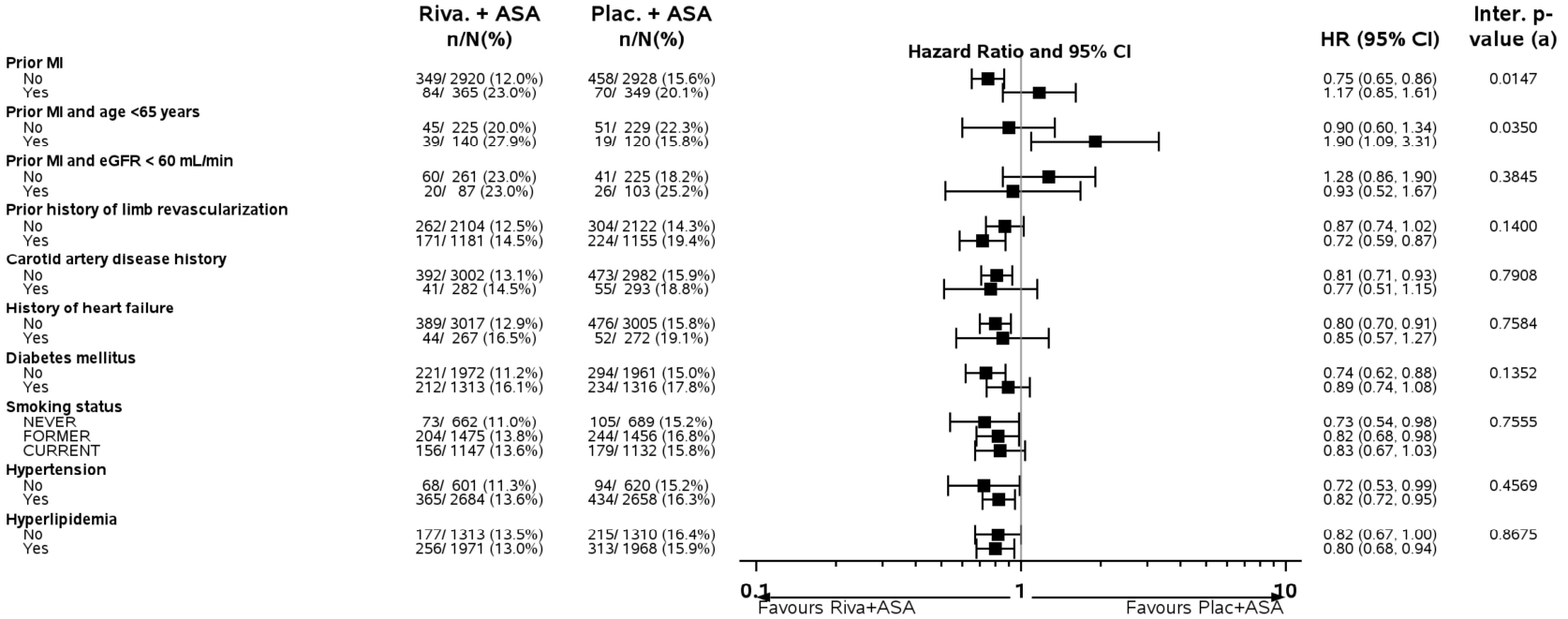
Figure displays outcome events meeting the definition as adjudicated by Independent Clinical Adjudication Committee (ICAC). Subgroup variables from Atrial fibrillation disease history and below are added post-hoc.
The ITT analysis set includes all randomized subjects. The ITT data scope includes outcome events observed from randomization date until efficacy cut-off date.
Subjects will be considered fragile if age >75 years or weight <=50 kg or baseline eGFR <50 mL/min/1.73m2. Efficacy cut-off date = 08SEP2019
bid = twice daily, od = once daily, ASA = acetylsalicylic acid, CI = confidence interval, Riva. + ASA = Rivaroxaban 2.5 mg bid + ASA 100 mg od, Plac. + ASA = Rivaroxaban placebo bid + ASA 100 mg od
n = number of subjects with events, N = number of subjects at risk, % = 100 * n/N., Inter. = Interaction
HR (95% CI) is based on the unstratified Cox proportional hazards model, with treatment as the only covariate
(a) P-value for interaction is based on the corresponding Cox proportional hazards model by adding the corresponding treatment interaction term.

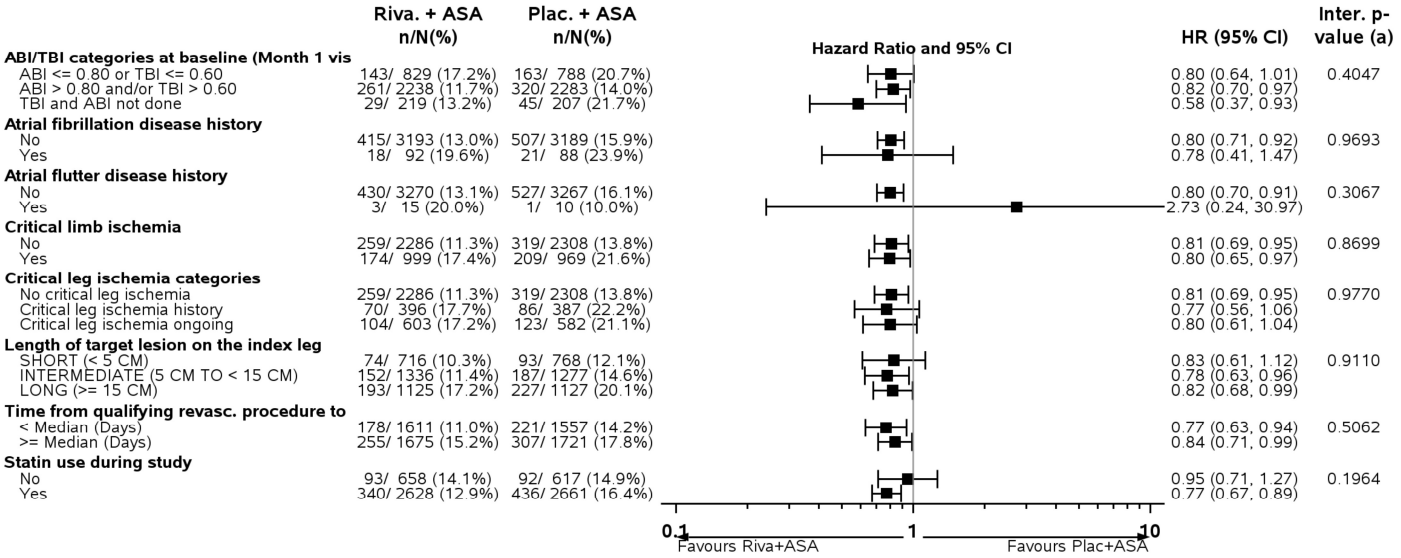
Source: 5.3.5.1.2 17454_J_analysis/Figure 14.2.5.1/4

図 2.7.3.7-2 MI、虚血性脳卒中、冠動脈性心疾患死、ALI、又は血管系の原因による大切断の複合エンドポイントの Forest プロット
（試験 17454、全体集団、ITT、ECOD まで、ICAC 判定）




Riva. + ASA n/N(%)
Plac. + ASA n/N(%)
Hazard Ratio and 95% CI
HR (95% CI)
Inter. p-value (a)
Clopidogrel use at the time of randomization
No 230/ 1621 (14.2%) 279/ 1613 (17.3%) 0.81 (0.68, 0.96)
Yes 202/ 1658 (12.2%) 248/ 1655 (15.0%) 0.80 (0.66, 0.96) 0.9400
Clopidogrel use continued after randomization (days)
None 230/ 1621 (14.2%) 279/ 1613 (17.3%) 0.81 (0.68, 0.96)
<= 30 days 126/ 988 (12.8%) 155/ 935 (16.6%) 0.74 (0.59, 0.94)
> 30 days 74/ 644 (11.5%) 88/ 678 (13.0%) 0.89 (0.66, 1.22) 0.6397
Geographic Region 1
North America 59/ 347 (17.0%) 58/ 347 (16.7%) 1.01 (0.70, 1.45)
Western Europe 102/ 914 (11.2%) 153/ 912 (16.8%) 0.64 (0.49, 0.82)
Eastern Europe 181/ 1301 (13.9%) 202/ 1298 (15.6%) 0.88 (0.72, 1.08)
Asia Pacific 56/ 481 (11.6%) 69/ 480 (14.4%) 0.82 (0.57, 1.16)
South America 35/ 243 (14.4%) 46/ 241 (19.1%) 0.78 (0.50, 1.21) 0.2204
Geographic Region 3
US 40/ 262 (15.3%) 38/ 262 (14.5%) 1.06 (0.68, 1.66)
non-US 393/ 3024 (13.0%) 490/ 3016 (16.2%) 0.78 (0.69, 0.90) 0.1980
Weight group (cut-off 60 kg)
<=60 kg 86/ 534 (16.1%) 100/ 547 (18.3%) 0.88 (0.66, 1.17)
>60 kg 344/ 2716 (12.7%) 422/ 2700 (15.6%) 0.80 (0.69, 0.92) 0.5607
eGFR (cut-offs: 60 ml/min/1.73m2)
<60 ml/min/1.73m2 100/ 661 (15.1%) 126/ 666 (18.9%) 0.81 (0.62, 1.05)
>=60 ml/min/1.73m2 316/ 2499 (12.6%) 378/ 2493 (15.2%) 0.81 (0.70, 0.94) 0.9876
eGFR (cut-offs: 15, 30 and 60 ml/min/1.73m2)
<15 ml/min/1.73m2 1/ 2 (50.0%) 0/ 0
15 - <30 ml/min/1.73m2 3/ 13 (23.1%) 5/ 28 (17.9%) 1.60 (0.35, 7.31)
30 - <60 ml/min/1.73m2 96/ 646 (14.9%) 121/ 638 (19.0%) 0.79 (0.60, 1.03)
>=60 ml/min/1.73m2 316/ 2499 (12.6%) 378/ 2493 (15.2%) 0.81 (0.70, 0.94) 0.5671
eGFR (cut-offs: 30, 50 and 80 ml/min/1.73m2)
<30 ml/min/1.73m2 4/ 15 (26.7%) 5/ 28 (17.9%) 2.44 (0.59, 10.12)
30 - 50 ml/min/1.73m2 47/ 343 (13.7%) 68/ 308 (22.1%) 0.61 (0.42, 0.89)
>50 - 80 ml/min/1.73m2 177/ 1367 (12.9%) 196/ 1369 (14.3%) 0.91 (0.74, 1.11)
>80 ml/min/1.73m2 188/ 1435 (13.1%) 235/ 1454 (16.2%) 0.77 (0.64, 0.93) 0.1250
Fragile subjects
No 292/ 2338 (12.5%) 348/ 2332 (14.9%) 0.81 (0.69, 0.95)
Yes 128/ 835 (15.3%) 158/ 839 (18.8%) 0.83 (0.65, 1.04) 0.8816
Prior coronary artery disease
No 269/ 2233 (12.0%) 331/ 2263 (14.6%) 0.81 (0.69, 0.96)
Yes 164/ 1052 (15.6%) 197/ 1015 (19.4%) 0.78 (0.64, 0.96) 0.7522
0.1
1
10
Favours Riva+ASA
Favours Plac+ASA


Riva. + ASA n/N(%)
Plac. + ASA n/N(%)
Hazard Ratio and 95% CI
HR (95% CI)
Inter. p-value (a)
Prior MI
No 349/ 2920 (12.0%) 458/ 2928 (15.6%) 0.75 (0.65, 0.86) 0.0147
Yes 84/ 365 (23.0%) 70/ 349 (20.1%) 1.17 (0.85, 1.61)
Prior MI and age <65 years
No 45/ 225 (20.0%) 51/ 229 (22.3%) 0.90 (0.60, 1.34) 0.0350
Yes 39/ 140 (27.9%) 19/ 120 (15.8%) 1.90 (1.09, 3.31)
Prior MI and eGFR < 60 mL/min
No 60/ 261 (23.0%) 41/ 225 (18.2%) 1.28 (0.86, 1.90) 0.3845
Yes 20/ 87 (23.0%) 26/ 103 (25.2%) 0.93 (0.52, 1.67)
Prior history of limb revascularization
No 262/ 2104 (12.5%) 304/ 2122 (14.3%) 0.87 (0.74, 1.02) 0.1400
Yes 171/ 1181 (14.5%) 224/ 1155 (19.4%) 0.72 (0.59, 0.87)
Carotid artery disease history
No 392/ 3002 (13.1%) 473/ 2982 (15.9%) 0.81 (0.71, 0.93) 0.7908
Yes 41/ 282 (14.5%) 55/ 293 (18.8%) 0.77 (0.51, 1.15)
History of heart failure
No 389/ 3017 (12.9%) 476/ 3005 (15.8%) 0.80 (0.70, 0.91) 0.7584
Yes 44/ 267 (16.5%) 52/ 272 (19.1%) 0.85 (0.57, 1.27)
Diabetes mellitus
No 221/ 1972 (11.2%) 294/ 1961 (15.0%) 0.74 (0.62, 0.88) 0.1352
Yes 212/ 1313 (16.1%) 234/ 1316 (17.8%) 0.89 (0.74, 1.08)
Smoking status
NEVER 73/ 662 (11.0%) 105/ 689 (15.2%) 0.73 (0.54, 0.98) 0.7555
FORMER 204/ 1475 (13.8%) 244/ 1456 (16.8%) 0.82 (0.68, 0.98)
CURRENT 156/ 1147 (13.6%) 179/ 1132 (15.8%) 0.83 (0.67, 1.03)
Hypertension
No 68/ 601 (11.3%) 94/ 620 (15.2%) 0.72 (0.53, 0.99) 0.4569
Yes 365/ 2684 (13.6%) 434/ 2658 (16.3%) 0.82 (0.72, 0.95)
Hyperlipidemia
No 177/ 1313 (13.5%) 215/ 1310 (16.4%) 0.82 (0.67, 1.00) 0.8675
Yes 256/ 1971 (13.0%) 313/ 1968 (15.9%) 0.80 (0.68, 0.94)
0.1
1
10
Favours Riva+ASA
Favours Plac+ASA



The ITT analysis set includes all randomized subjects. The ITT data scope includes outcome events observed from randomization date until efficacy cut-off date. Subgroup variables from Atrial fibrillation disease history and below are added post-hoc.
MI, stroke, mortality, ALI, major amputation of vascular etiology and events leading to hospitalization are adjudicated by Independent Clinical Adjudication Committee (ICAC), index limb revascularization and venous thromboembolic events are reported by investigator only. Index limb revascularization is defined as subsequent index leg revascularization that was not planned or considered as part of the initial treatment plan at the time of randomization, CV death = Cardiovascular death and unknown cause, MI = Myocardial infarction, ALI = Acute limb ischemia, CHD = coronary heart disease. Efficacy cut-off date = 08SEP2019,
Subjects will be considered fragile if age >75 years or weight <=50 kg or baseline eGFR <50 mL/min/1.73m2.
bid = twice daily, od = once daily, ASA = acetylsalicylic acid, CI = confidence interval, Riva. + ASA = Rivaroxaban 2.5 mg bid + ASA 100 mg od, Plac. + ASA = Rivaroxaban placebo bid + ASA 100 mg od
n = number of subjects with events, N = number of subjects at risk, % = 100 * n/N. Inter. = Interaction
HR (95% CI) is based on the Cox proportional hazards model stratified by type of procedure and clopidogrel use (per IxRS) (except for subgroups related to qualifying revascularization procedure or clopidogrel use), with treatment as the only covariate.
(a) P-value for interaction is based on the Cox proportional hazards model stratified by type of procedure and clopidogrel use (per IxRS) by adding the corresponding treatment interaction term.

Source: 5.3.5.1.1 PH-40164/Figure 14.2.5.2/1