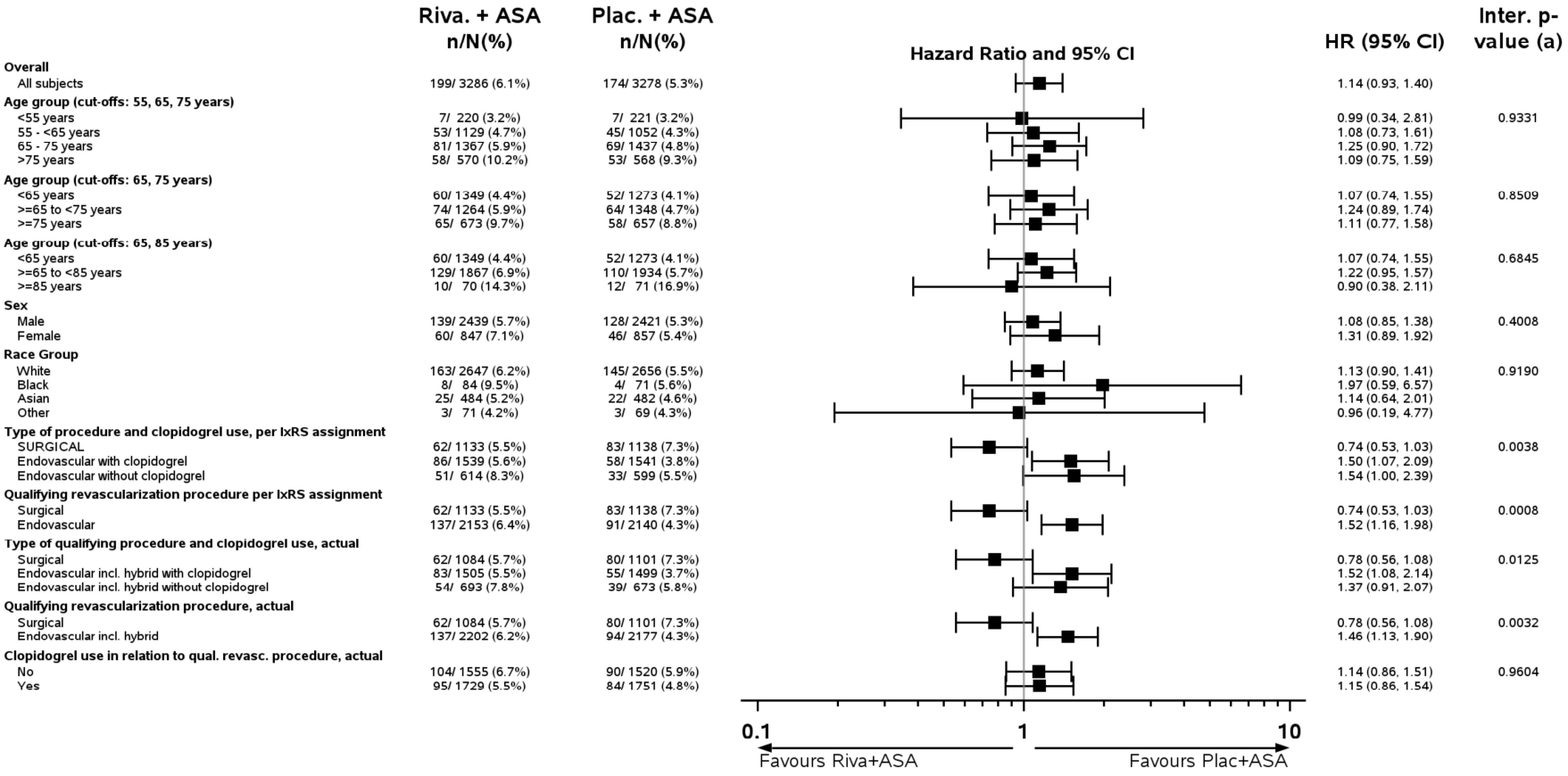
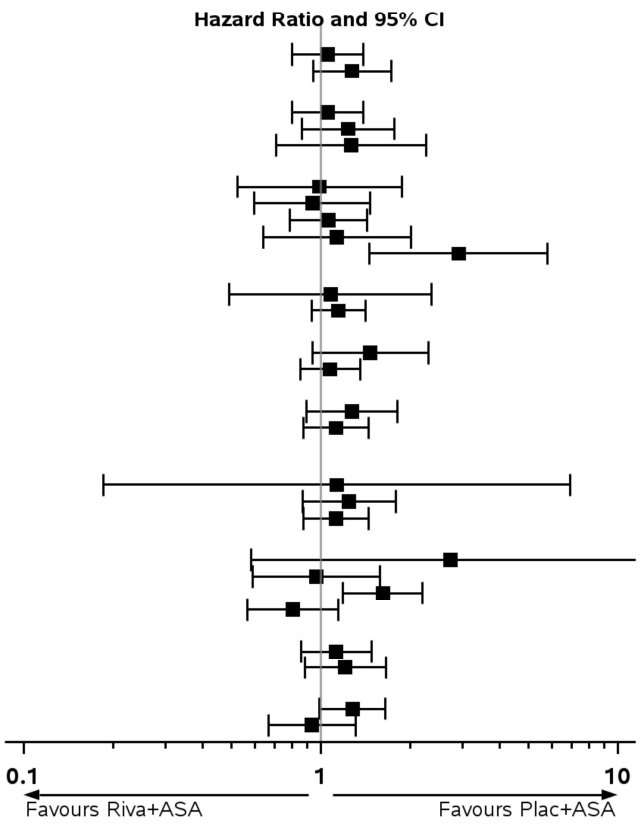
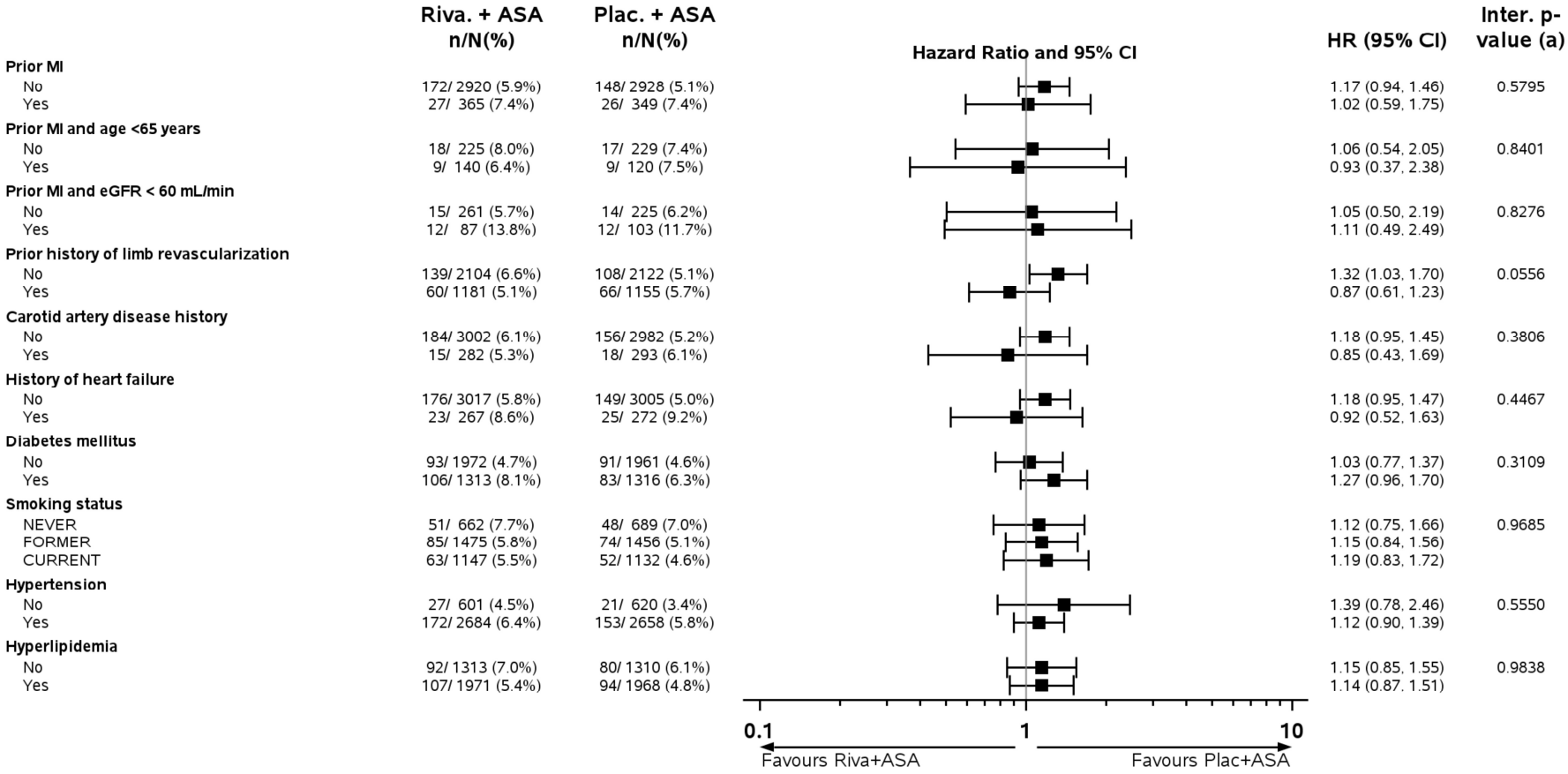
図 2.7.3.7-14　心血管死の Forest プロット（試験 17454、全体集団、ITT、ECOD まで、ICAC 判定）



	Riva. + ASA n/N(%)	Plac. + ASA n/N(%)	HR (95% CI)	Inter. p-value (a)
Clopidogrel use at the time of randomization				
No	104/ 1621 (6.4%)	98/ 1613 (6.1%)	1.06 (0.80, 1.39)	0.3745
Yes	95/ 1658 (5.7%)	75/ 1655 (4.5%)	1.27 (0.94, 1.72)	
Clopidogrel use continued after randomization (days)				
None	104/ 1621 (6.4%)	98/ 1613 (6.1%)	1.06 (0.80, 1.39)	0.7300
<= 30 days	69/ 988 (7.0%)	53/ 935 (5.7%)	1.24 (0.87, 1.77)	
> 30 days	25/ 644 (3.9%)	21/ 678 (3.1%)	1.27 (0.71, 2.26)	
Geographic Region 1				
North America	19/ 347 (5.5%)	19/ 347 (5.5%)	0.99 (0.52, 1.87)	0.0913
Western Europe	37/ 914 (4.0%)	39/ 912 (4.3%)	0.94 (0.60, 1.47)	
Eastern Europe	88/ 1301 (6.8%)	83/ 1298 (6.4%)	1.06 (0.79, 1.43)	
Asia Pacific	25/ 481 (5.2%)	22/ 480 (4.6%)	1.13 (0.64, 2.01)	
South America	30/ 243 (12.3%)	11/ 241 (4.6%)	2.91 (1.46, 5.81)	
Geographic Region 3				
US	13/ 262 (5.0%)	12/ 262 (4.6%)	1.08 (0.49, 2.36)	0.8748
non-US	186/ 3024 (6.2%)	162/ 3016 (5.4%)	1.15 (0.93, 1.42)	
Weight group (cut-off 60 kg)				
<=60 kg	46/ 534 (8.6%)	32/ 547 (5.9%)	1.47 (0.94, 2.31)	0.2217
>60 kg	150/ 2716 (5.5%)	139/ 2700 (5.1%)	1.07 (0.85, 1.35)	
eGFR (cut-offs: 60 ml/min/1.73m2)				
<60 ml/min/1.73m2	69/ 661 (10.4%)	56/ 666 (8.4%)	1.27 (0.89, 1.81)	0.5693
>=60 ml/min/1.73m2	127/ 2499 (5.1%)	112/ 2493 (4.5%)	1.13 (0.87, 1.45)	
eGFR (cut-offs: 15, 30 and 60 ml/min/1.73m2)				
<15 ml/min/1.73m2	2/ 2 (100.0%)	0/ 0		0.8816
15 - <30 ml/min/1.73m2	2/ 13 (15.4%)	3/ 28 (10.7%)	1.13 (0.18, 6.91)	
30 - <60 ml/min/1.73m2	65/ 646 (10.1%)	53/ 638 (8.3%)	1.25 (0.87, 1.79)	
>=60 ml/min/1.73m2	127/ 2499 (5.1%)	112/ 2493 (4.5%)	1.13 (0.87, 1.45)	
eGFR (cut-offs: 30, 50 and 80 ml/min/1.73m2)				
<30 ml/min/1.73m2	4/ 15 (26.7%)	3/ 28 (10.7%)	2.73 (0.58, 12.80)	0.0175
30 - 50 ml/min/1.73m2	33/ 343 (9.6%)	31/ 308 (10.1%)	0.97 (0.59, 1.58)	
>50 - 80 ml/min/1.73m2	103/ 1367 (7.5%)	65/ 1369 (4.7%)	1.61 (1.18, 2.20)	
>80 ml/min/1.73m2	56/ 1435 (3.9%)	69/ 1454 (4.7%)	0.81 (0.57, 1.15)	
Fragile subjects				
No	110/ 2338 (4.7%)	97/ 2332 (4.2%)	1.13 (0.86, 1.48)	0.7066
Yes	86/ 835 (10.3%)	72/ 839 (8.6%)	1.21 (0.88, 1.66)	
Prior coronary artery disease				
No	133/ 2233 (6.0%)	106/ 2263 (4.7%)	1.28 (0.99, 1.65)	0.1424
Yes	66/ 1052 (6.3%)	68/ 1015 (6.7%)	0.93 (0.67, 1.31)	




Riva. + ASA n/N(%)
Plac. + ASA n/N(%)
Hazard Ratio and 95% CI
HR (95% CI)
Inter. p-value (a)
Prior MI
No 172/ 2920 (5.9%) 148/ 2928 (5.1%) 1.17 (0.94, 1.46) 0.5795
Yes 27/ 365 (7.4%) 26/ 349 (7.4%) 1.02 (0.59, 1.75)
Prior MI and age <65 years
No 18/ 225 (8.0%) 17/ 229 (7.4%) 1.06 (0.54, 2.05) 0.8401
Yes 9/ 140 (6.4%) 9/ 120 (7.5%) 0.93 (0.37, 2.38)
Prior MI and eGFR < 60 mL/min
No 15/ 261 (5.7%) 14/ 225 (6.2%) 1.05 (0.50, 2.19) 0.8276
Yes 12/ 87 (13.8%) 12/ 103 (11.7%) 1.11 (0.49, 2.49)
Prior history of limb revascularization
No 139/ 2104 (6.6%) 108/ 2122 (5.1%) 1.32 (1.03, 1.70) 0.0556
Yes 60/ 1181 (5.1%) 66/ 1155 (5.7%) 0.87 (0.61, 1.23)
Carotid artery disease history
No 184/ 3002 (6.1%) 156/ 2982 (5.2%) 1.18 (0.95, 1.45) 0.3806
Yes 15/ 282 (5.3%) 18/ 293 (6.1%) 0.85 (0.43, 1.69)
History of heart failure
No 176/ 3017 (5.8%) 149/ 3005 (5.0%) 1.18 (0.95, 1.47) 0.4467
Yes 23/ 267 (8.6%) 25/ 272 (9.2%) 0.92 (0.52, 1.63)
Diabetes mellitus
No 93/ 1972 (4.7%) 91/ 1961 (4.6%) 1.03 (0.77, 1.37) 0.3109
Yes 106/ 1313 (8.1%) 83/ 1316 (6.3%) 1.27 (0.96, 1.70)
Smoking status
NEVER 51/ 662 (7.7%) 48/ 689 (7.0%) 1.12 (0.75, 1.66) 0.9685
FORMER 85/ 1475 (5.8%) 74/ 1456 (5.1%) 1.15 (0.84, 1.56)
CURRENT 63/ 1147 (5.5%) 52/ 1132 (4.6%) 1.19 (0.83, 1.72)
Hypertension
No 27/ 601 (4.5%) 21/ 620 (3.4%) 1.39 (0.78, 2.46) 0.5550
Yes 172/ 2684 (6.4%) 153/ 2658 (5.8%) 1.12 (0.90, 1.39)
Hyperlipidemia
No 92/ 1313 (7.0%) 80/ 1310 (6.1%) 1.15 (0.85, 1.55) 0.9838
Yes 107/ 1971 (5.4%) 94/ 1968 (4.8%) 1.14 (0.87, 1.51)
0.1
1
10
Favours Riva+ASA
Favours Plac+ASA

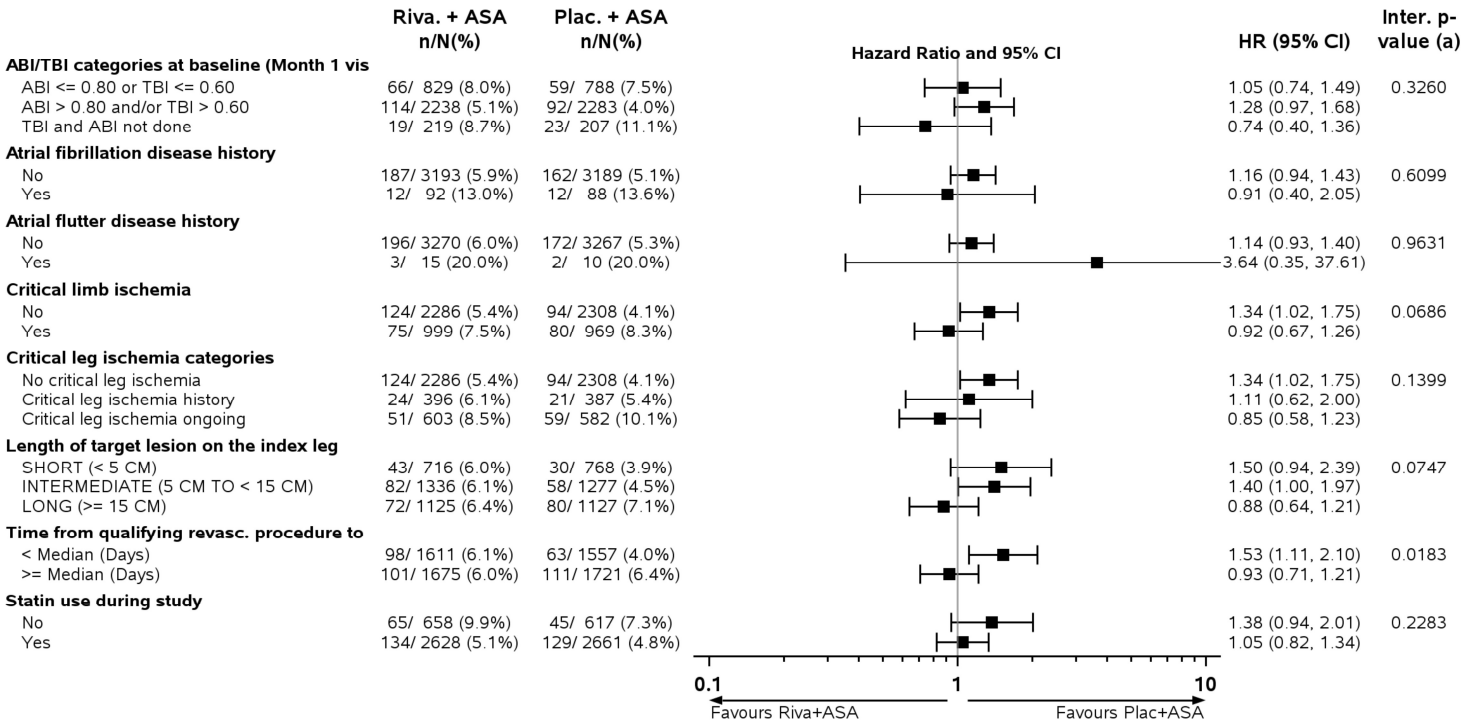
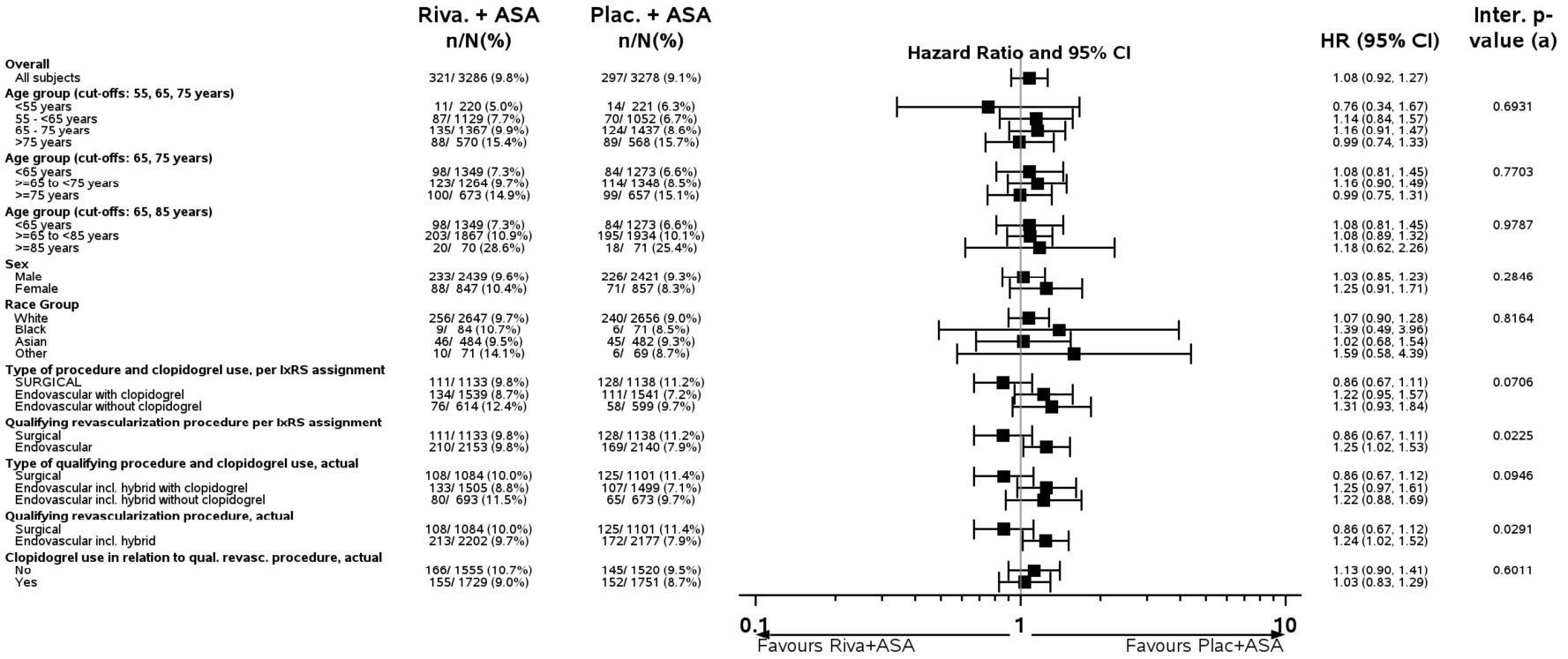
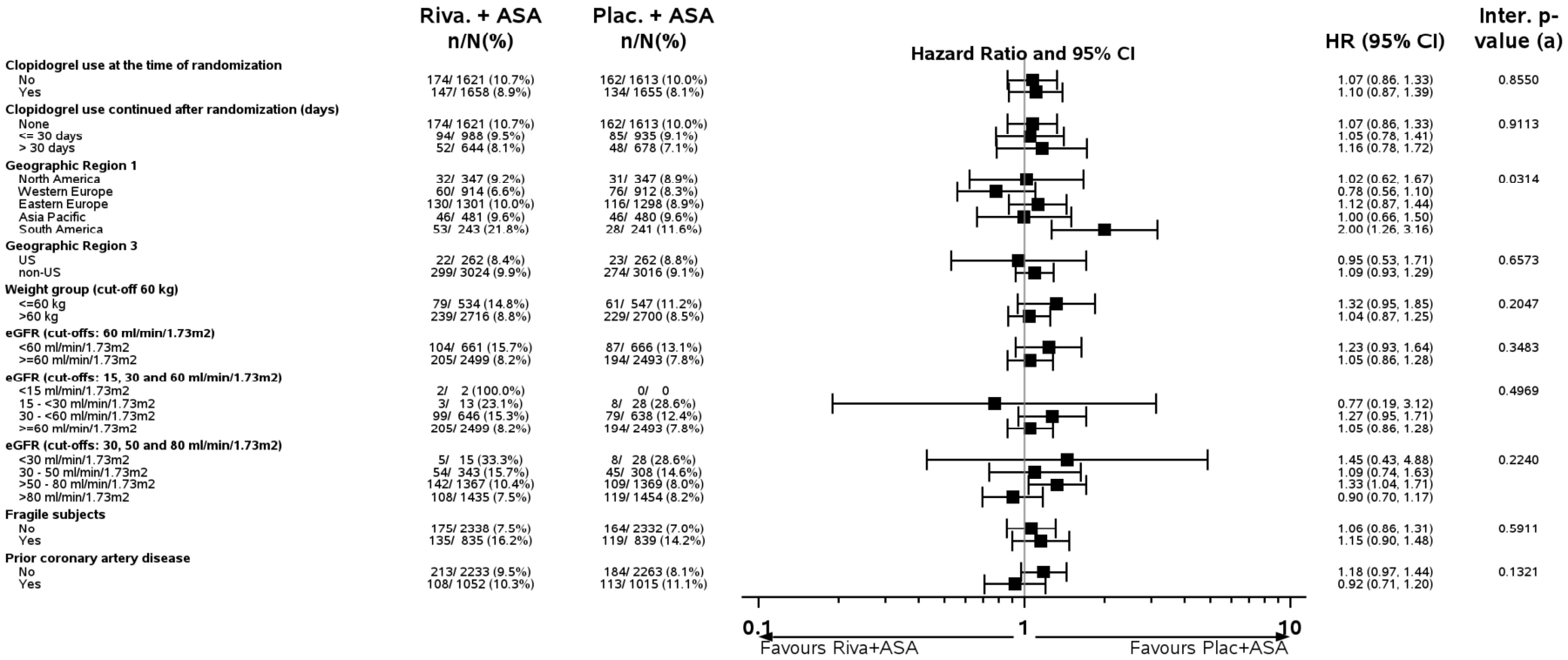


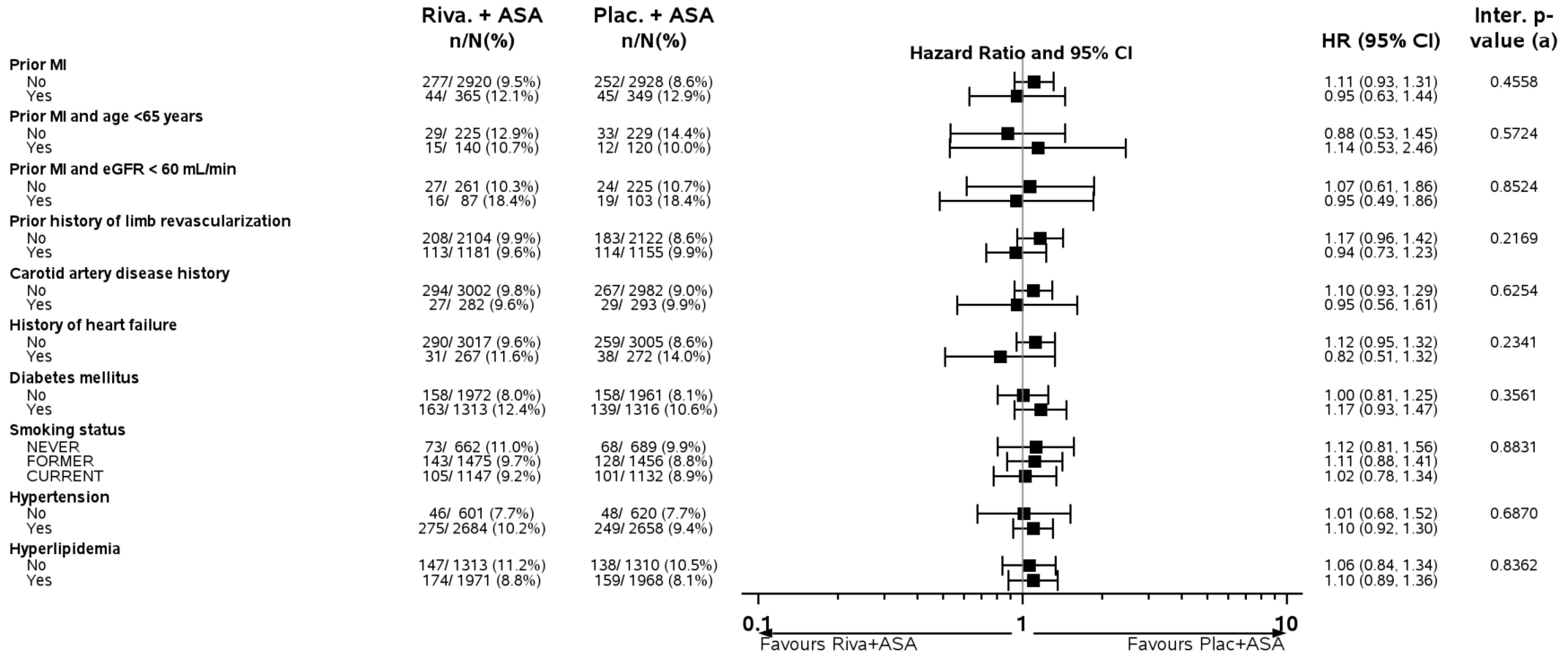
Figure displays outcome events meeting the definition as adjudicated by Independent Clinical Adjudication Committee (ICAC). Subgroup variables from Atrial fibrillation disease history and below are added post-hoc.
The ITT analysis set includes all randomized subjects. The ITT data scope includes outcome 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 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.

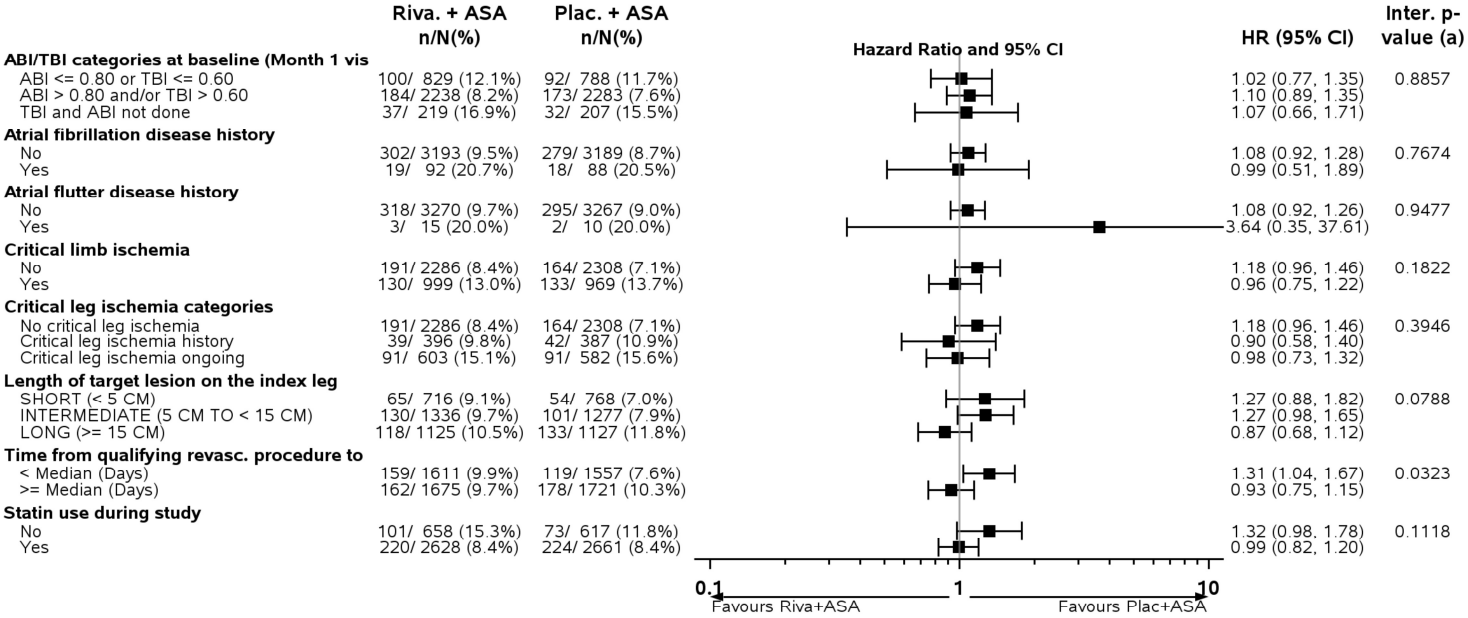
Source: 5.3.5.1.1 PH-40164/Figure 14.2.5.1/5

図 2.7.3.7-15　全死亡の 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 174/ 1621 (10.7%) 162/ 1613 (10.0%) 1.07 (0.86, 1.33) 0.8550
Yes 147/ 1658 (8.9%) 134/ 1655 (8.1%) 1.10 (0.87, 1.39)
Clopidogrel use continued after randomization (days)
None 174/ 1621 (10.7%) 162/ 1613 (10.0%) 1.07 (0.86, 1.33) 0.9113
<= 30 days 94/ 988 (9.5%) 85/ 935 (9.1%) 1.05 (0.78, 1.41)
> 30 days 52/ 644 (8.1%) 48/ 678 (7.1%) 1.16 (0.78, 1.72)
Geographic Region 1
North America 32/ 347 (9.2%) 31/ 347 (8.9%) 1.02 (0.62, 1.67) 0.0314
Western Europe 60/ 914 (6.6%) 76/ 912 (8.3%) 0.78 (0.56, 1.10)
Eastern Europe 130/ 1301 (10.0%) 116/ 1298 (8.9%) 1.12 (0.87, 1.44)
Asia Pacific 46/ 481 (9.6%) 46/ 480 (9.6%) 1.00 (0.66, 1.50)
South America 53/ 243 (21.8%) 28/ 241 (11.6%) 2.00 (1.26, 3.16)
Geographic Region 3
US 22/ 262 (8.4%) 23/ 262 (8.8%) 0.95 (0.53, 1.71) 0.6573
non-US 299/ 3024 (9.9%) 274/ 3016 (9.1%) 1.09 (0.93, 1.29)
Weight group (cut-off 60 kg)
<=60 kg 79/ 534 (14.8%) 61/ 547 (11.2%) 1.32 (0.95, 1.85) 0.2047
>60 kg 239/ 2716 (8.8%) 229/ 2700 (8.5%) 1.04 (0.87, 1.25)
eGFR (cut-offs: 60 ml/min/1.73m2)
<60 ml/min/1.73m2 104/ 661 (15.7%) 87/ 666 (13.1%) 1.23 (0.93, 1.64) 0.3483
>=60 ml/min/1.73m2 205/ 2499 (8.2%) 194/ 2493 (7.8%) 1.05 (0.86, 1.28)
eGFR (cut-offs: 15, 30 and 60 ml/min/1.73m2)
<15 ml/min/1.73m2 2/ 2 (100.0%) 0/ 0 0.4969
15 - <30 ml/min/1.73m2 3/ 13 (23.1%) 8/ 28 (28.6%) 0.77 (0.19, 3.12)
30 - <60 ml/min/1.73m2 99/ 646 (15.3%) 79/ 638 (12.4%) 1.27 (0.95, 1.71)
>=60 ml/min/1.73m2 205/ 2499 (8.2%) 194/ 2493 (7.8%) 1.05 (0.86, 1.28)
eGFR (cut-offs: 30, 50 and 80 ml/min/1.73m2)
<30 ml/min/1.73m2 5/ 15 (33.3%) 8/ 28 (28.6%) 1.45 (0.43, 4.88) 0.2240
30 - 50 ml/min/1.73m2 54/ 343 (15.7%) 45/ 308 (14.6%) 1.09 (0.74, 1.63)
>50 - 80 ml/min/1.73m2 142/ 1367 (10.4%) 109/ 1369 (8.0%) 1.33 (1.04, 1.71)
>80 ml/min/1.73m2 108/ 1435 (7.5%) 119/ 1454 (8.2%) 0.90 (0.70, 1.17)
Fragile subjects
No 175/ 2338 (7.5%) 164/ 2332 (7.0%) 1.06 (0.86, 1.31) 0.5911
Yes 135/ 835 (16.2%) 119/ 839 (14.2%) 1.15 (0.90, 1.48)
Prior coronary artery disease
No 213/ 2233 (9.5%) 184/ 2263 (8.1%) 1.18 (0.97, 1.44) 0.1321
Yes 108/ 1052 (10.3%) 113/ 1015 (11.1%) 0.92 (0.71, 1.20)
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 277/ 2920 (9.5%) 252/ 2928 (8.6%) 1.11 (0.93, 1.31) 0.4558
Yes 44/ 365 (12.1%) 45/ 349 (12.9%) 0.95 (0.63, 1.44)
Prior MI and age <65 years
No 29/ 225 (12.9%) 33/ 229 (14.4%) 0.88 (0.53, 1.45) 0.5724
Yes 15/ 140 (10.7%) 12/ 120 (10.0%) 1.14 (0.53, 2.46)
Prior MI and eGFR < 60 mL/min
No 27/ 261 (10.3%) 24/ 225 (10.7%) 1.07 (0.61, 1.86) 0.8524
Yes 16/ 87 (18.4%) 19/ 103 (18.4%) 0.95 (0.49, 1.86)
Prior history of limb revascularization
No 208/ 2104 (9.9%) 183/ 2122 (8.6%) 1.17 (0.96, 1.42) 0.2169
Yes 113/ 1181 (9.6%) 114/ 1155 (9.9%) 0.94 (0.73, 1.23)
Carotid artery disease history
No 294/ 3002 (9.8%) 267/ 2982 (9.0%) 1.10 (0.93, 1.29) 0.6254
Yes 27/ 282 (9.6%) 29/ 293 (9.9%) 0.95 (0.56, 1.61)
History of heart failure
No 290/ 3017 (9.6%) 259/ 3005 (8.6%) 1.12 (0.95, 1.32) 0.2341
Yes 31/ 267 (11.6%) 38/ 272 (14.0%) 0.82 (0.51, 1.32)
Diabetes mellitus
No 158/ 1972 (8.0%) 158/ 1961 (8.1%) 1.00 (0.81, 1.25) 0.3561
Yes 163/ 1313 (12.4%) 139/ 1316 (10.6%) 1.17 (0.93, 1.47)
Smoking status
NEVER 73/ 662 (11.0%) 68/ 689 (9.9%) 1.12 (0.81, 1.56) 0.8831
FORMER 143/ 1475 (9.7%) 128/ 1456 (8.8%) 1.11 (0.88, 1.41)
CURRENT 105/ 1147 (9.2%) 101/ 1132 (8.9%) 1.02 (0.78, 1.34)
Hypertension
No 46/ 601 (7.7%) 48/ 620 (7.7%) 1.01 (0.68, 1.52) 0.6870
Yes 275/ 2684 (10.2%) 249/ 2658 (9.4%) 1.10 (0.92, 1.30)
Hyperlipidemia
No 147/ 1313 (11.2%) 138/ 1310 (10.5%) 1.06 (0.84, 1.34) 0.8362
Yes 174/ 1971 (8.8%) 159/ 1968 (8.1%) 1.10 (0.89, 1.36)
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 14.2.5.2/8