COMPASS

Presenter Disclosure Information

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The Effect of Rivaroxaban with Aspirin on Stroke Outcomes in the Cardiovascular Outcomes for People Using Anticoagulation Strategies (COMPASS) Trial

FINANCIAL DISCLOSURE:
Research grant (significant) COMPASS was funded by Bayer
Consultant (modest) Bayer, BMS, BI, Daiichi Sankyo

UNLABELED/UNAPPROVED USES DISCLOSURE:
Rivaroxaban with aspirin for the prevention of vascular events

COMPASS

The Effect of Rivaroxaban with Aspirin on Stroke Outcomes in the Cardiovascular OutcoMes for People Using Anticoagulation StrategieS (COMPASS) Trial

Mike Sharma MD, On behalf of the COMPASS
Steering Committee and Investigators

January 25, 2018

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Background

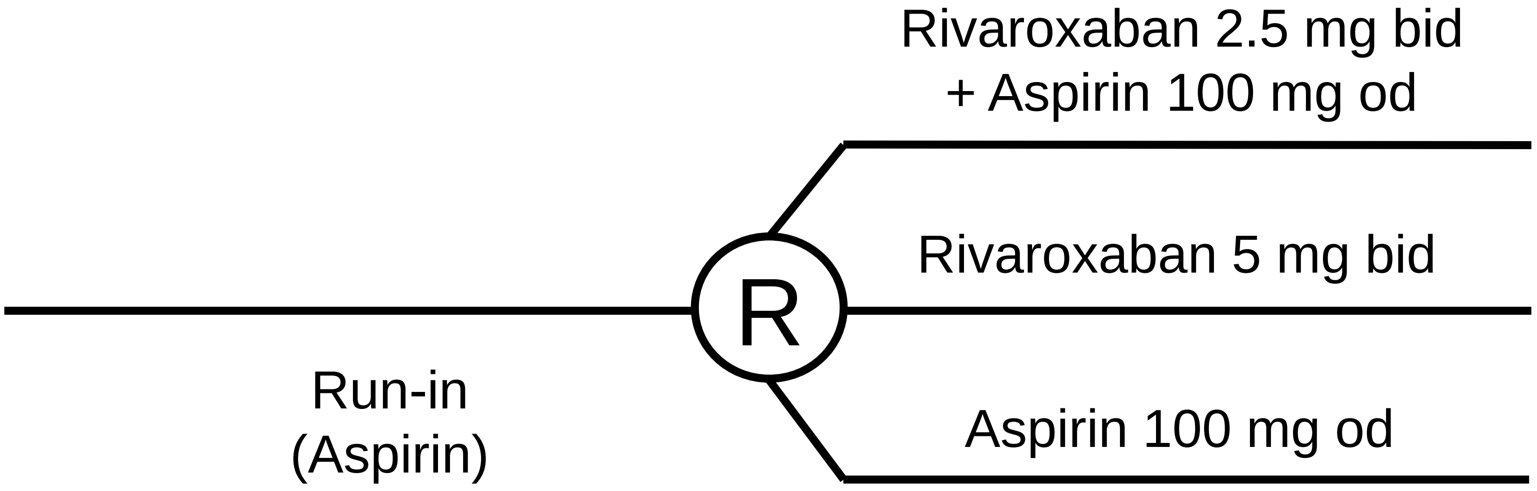
- Patients with cardiovascular disease
  - CV events 5-10% per year

    - Aspirin
      - RRR 12% primary prevention
      - RRR 19% secondary prevention

***Lancet* 2009;373(9678):1849-60**

COMPASS Design

- N = 27,395 coronary artery or peripheral artery disease
  - Primary outcome: stroke, MI, cardiovascular death
  - 1,323 participants with a primary outcome event



Rivaroxaban 2.5 mg bid
+ Aspirin 100 mg od

Rivaroxaban 5 mg bid

Aspirin 100 mg od

Run-in
(Aspirin)

Mean follow up: 1.9 years

N Engl J Med 2017; 377: 1319-30.

COMPASS Design

- Main Inclusion Criteria
  - Coronary artery disease:
    - MI within 20 years or multivessel disease
  - Peripheral Artery Disease:
    - Surgery for PAD including amputation
    - Intermittent claudication plus
      - Carotid stenosis ≥ 50% (asymptomatic)
      - Carotid revascularization

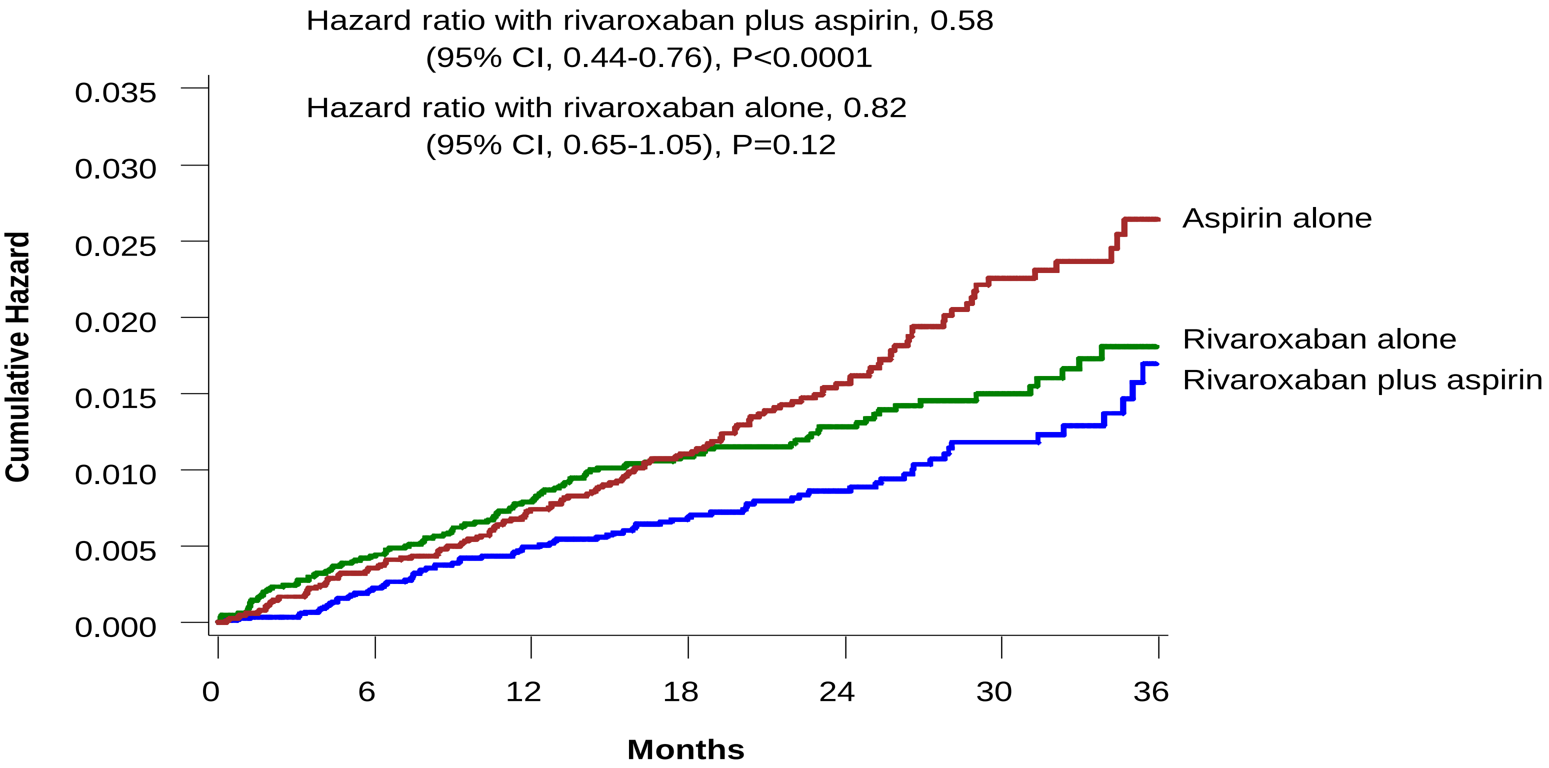
- Relevant Exclusion Criteria
  - Stroke within 1 month
  - Symptomatic lacunar stroke
    - Asymptomatic lacunes permitted
  - Intracerebral hemorrhage
  - Atrial Fibrillation

Primary: CV death, stroke, MI

Outcome	R + A N=9,152	R N=9,117	A N=9,126	Rivaroxaban + aspirin vs. aspirin		Rivaroxaban vs. aspirin	
	N (%)	N (%)	N (%)	HR (95% CI)	p	HR (95% CI)	p
CV death, stroke, MI	379 (4.1%)	448 (4.9%)	496 (5.4%)	0.76 (0.66-0.86)	<0.0001	0.90 (0.79-1.03)	0.12

Stroke

Stroke


Hazard ratio with rivaroxaban plus aspirin, 0.58
(95% CI, 0.44-0.76), P<0.0001

Hazard ratio with rivaroxaban alone, 0.82
(95% CI, 0.65-1.05), P=0.12

No. at Risk

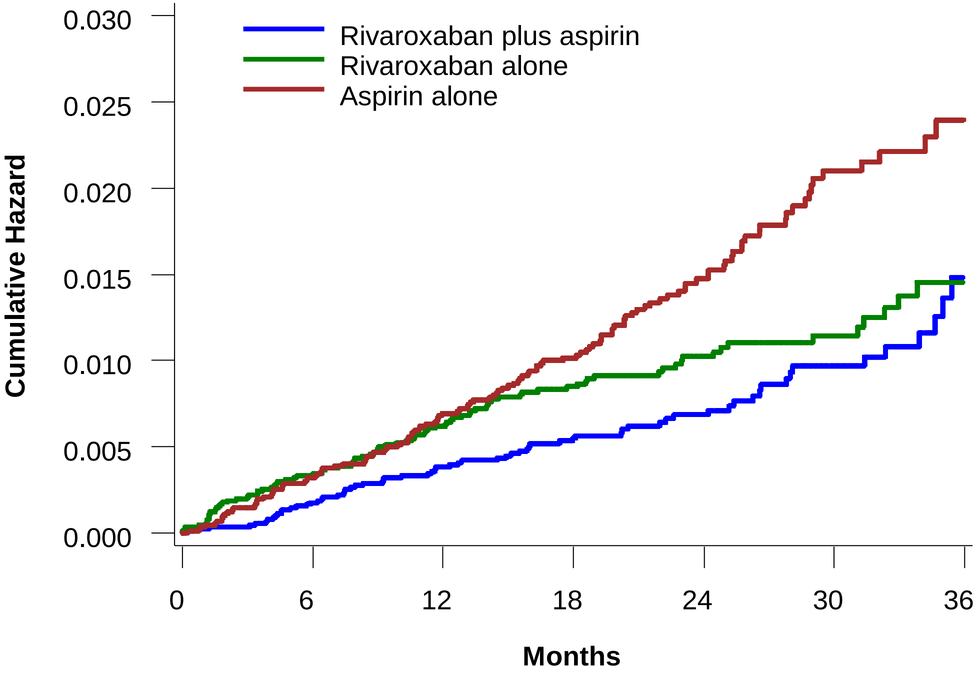
Rivaroxaban plus aspirin	9152	9067	7969	6370	3970	2256	673
Rivaroxaban alone	9117	9010	7889	6279	3935	2221	686
Aspirin alone	9126	9019	7870	6245	3948	2228	691

Ischemic/Uncertain Stroke

A Ischemic or Uncertain Stroke

HR Riva plus aspirin
0.51
(95% CI, 0.38-0.69)

HR Riva alone
0.66
(95% CI, 0.50-0.88)



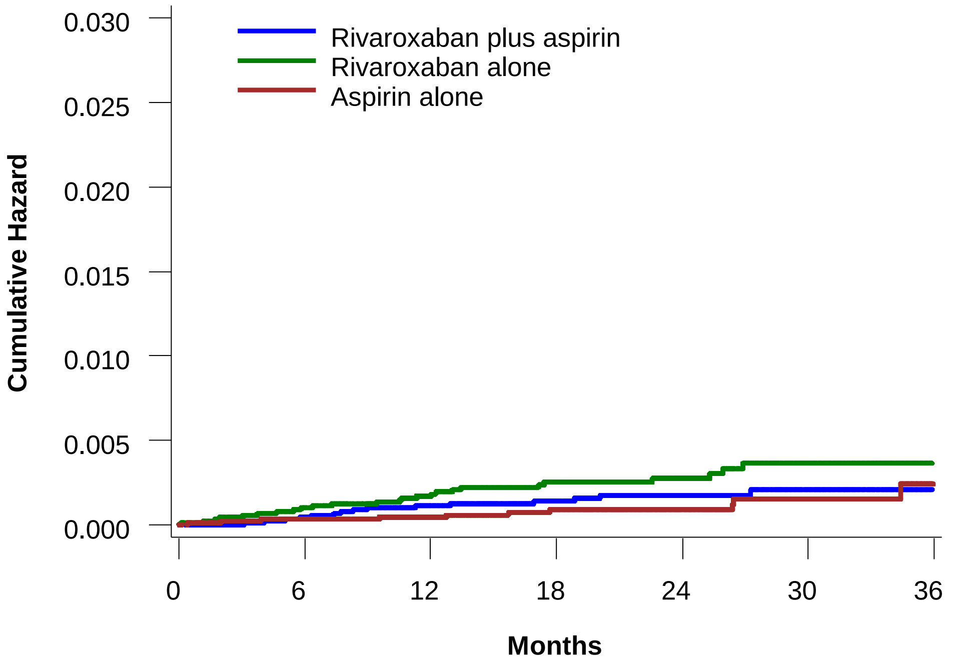
No. at Risk							
Rivaroxaban plus aspirin	9152	9069	7973	6374	3975	2259	673
Rivaroxaban alone	9117	9016	7898	6291	3943	2228	691
Aspirin alone	9126	9022	7874	6251	3951	2231	693

Hemorrhagic Stroke

HR Riva plus aspirin
1.49
(95% CI, 0.67-3.31)

HR Riva alone
2.70
(95% CI, 1.31-5.58)

B Hemorrhagic Stroke



No. at Risk							
Rivaroxaban plus aspirin	9152	9082	7996	6405	3998	2279	679
Rivaroxaban alone	9117	9034	7932	6320	3972	2243	692
Aspirin alone	9126	9047	7922	6303	4005	2273	703

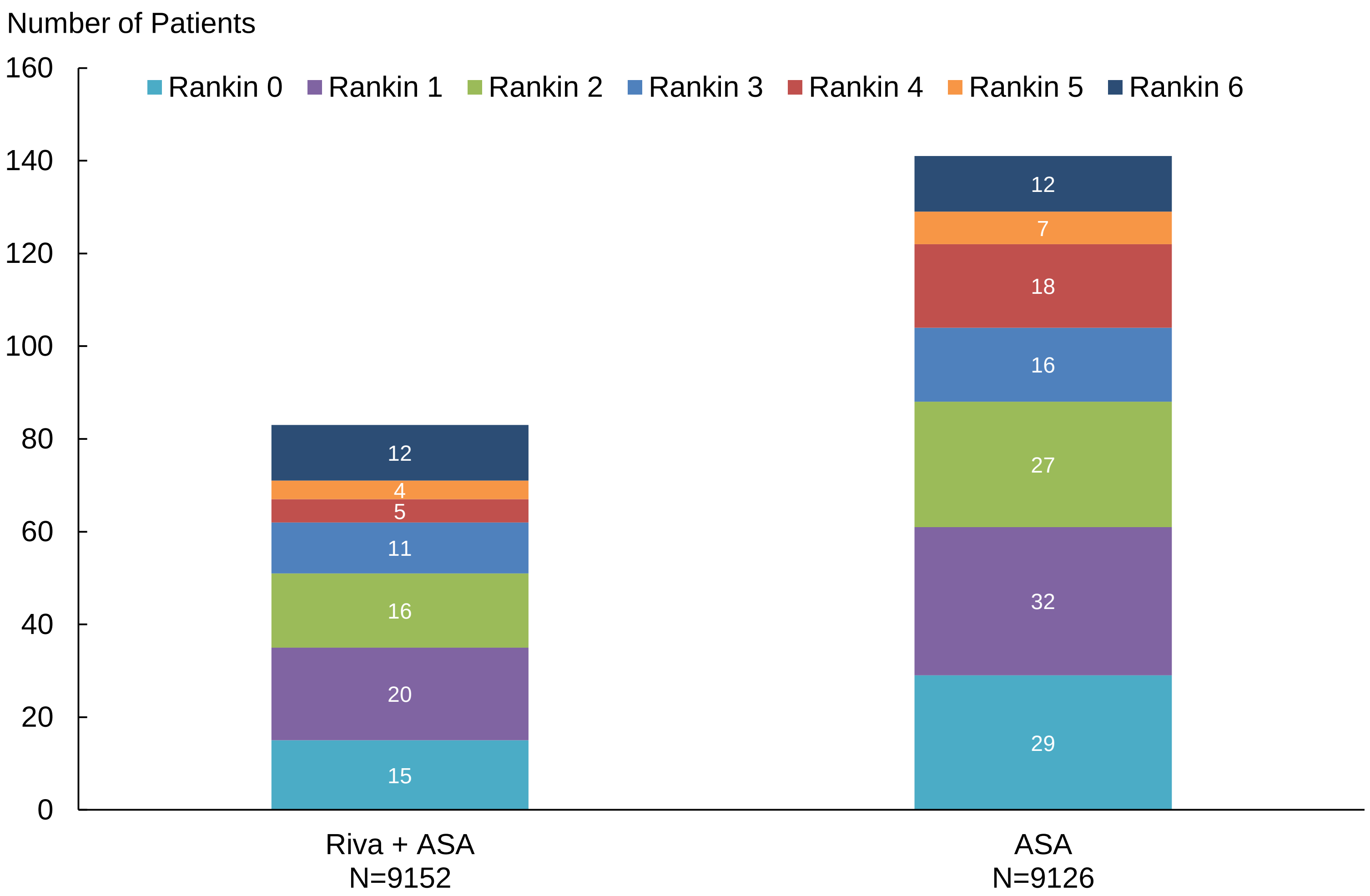
Stroke Outcomes by Treatment

	Rivaroxaban plus Aspirin (N=9152)		Aspirin (N=9126)		Rivaroxaban plus Aspirin vs. Aspirin	
	N	%/yr	N	%/yr	HR (95% CI)	P
Stroke	83	0.5	142	0.8	0.58 (0.44-0.76)	<0.0001
Ischemic stroke	64	0.4	125	0.7	0.51 (0.38-0.69)	<0.0001
Hemorrhagic transformation	5	0.03	14	0.08	0.35 (0.13-0.99)	0.04
Hemorrhagic stroke	15	0.09	10	0.06	1.49 (0.67-3.31)	0.33
Death within 30 days of stroke	11	0.06	13	0.07	0.84 (0.38-1.88)	0.68

mRS at 7 Days or Hospital Discharge

	Rivaroxaban plus Aspirin (N=9152)		Aspirin (N=9126)		Rivaroxaban plus Aspirin vs. Aspirin	
	N	%/yr	N	%/yr	HR (95% CI)	P
Stroke						
0-2	51	0.3	90	0.5	0.56 (0.40-0.79)	0.001
3-6	32	0.2	55	0.3	0.58 (0.37-0.89)	0.01
Ischemic/uncertain						
0-2	46	0.3	82	0.5	0.56 (0.39-0.80)	0.001
3-6	22	0.1	51	0.3	0.43 (0.26-0.71)	0.0006
Hemorrhagic stroke						
0-2	5	0.03	8	0.05	0.62 (0.20-1.89)	0.40
3-6	10	0.06	4	0.02	2.48 (0.78-7.92)	0.11

mRS at 7 Days or Hospital Discharge



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Selected Predictors of Stroke

Characteristic	N Pts (% of cohort)	Stroke			Ischemic/Uncertain			Hemorrhagic		
		%/yr	HR (95%CI)	P	%/yr	HR (95%CI)	P	%/yr	HR (95%CI)	P
Prev stroke	1,032 (3.8)	2.6	4.43 (3.25-6.02)	0.0001	2.4	4.82 (3.48-6.66)	0.0001	0.3	2.88 (1.14-7.23)	0.02
Prev MI	17,028 (62.2)	0.7	1.00 (0.81-1.25)	0.98	0.6	1.02 (0.80-1.23)	0.87	0.09	0.87 (0.50-1.51)	0.62
Asymptomatic Carotid stenosis ≥ 50% or revascularization	1919 (7.0)	0.9	1.40 (0.97-2.03)	0.07	0.9	1.68 (1.16-2.44)	0.006	0.03	0.28 (0.04-1.99)	0.20
Race										
White	17027	0.6	Ref	0.001	0.5	Ref	0.02	0.08	Ref	0.01
Black	262	0.2	0.36 (0.05-2.55)		0.2	0.41 (0.06-2.96)		0	n/a	
Asian	4269	1.0	1.66 (1.28-2.15)		0.8	1.55 (1.16-2.06)		0.2	2.47 (1.34-4.53)	
Other	5837	0.6	1.18 (0.89-1.55)		0.6	1.21 (0.9-1.62)		0.08	0.98 (0.44-2.16)	

Age, hypertension, diabetes also predict stroke

Previous Stroke Status and Outcomes

Outcome	Rivaroxaban plus Aspirin (N=9152)		Aspirin (N=9126)		Rivaroxaban plus Aspirin vs. Aspirin		
	N Pts	%/yr	N Pts	%/yr	HR (95% CI)	P	P inter
Stroke							0.40
No Previous Stroke	8801	0.4	8791	0.7	0.60 (0.45-0.80)	0.0006	
Previous Stroke	351	0.7	335	3.4	0.42 (0.19-0.92)	0.03	
Ischemic or uncertain stroke							0.28
No Previous Stroke	8801	0.4	8791	0.7	0.54 (0.40-0.74)	0.0001	
Previous Stroke	351	1.1	335	3.4	0.33 (0.14-0.77)	0.01	

Previous stroke ARR = 2.7%

NNT = 37

Conclusions

- Rivaroxaban 2.5 mg BID + aspirin compared to aspirin
  - Reduced ischemic stroke by 49%
    - Without a significant increase in ICH
    - Or hemorrhagic conversion
  - Major effect in secondary prevention*
    - Stroke: ARR 2.7%, NNT = 37
  - Reduced early disability
    - Commensurate with decrease in stroke occurrence
- A significant advance in stroke prevention for those with CAD/PAD without AF

* Stroke within 1 month exclusion