

# AVERROES

## *Apixaban Versus ASA To Reduce the Risk Of Stroke*

Coordinated by Population Health Research institute  
Hamilton, Ontario, Canada

Sponsors: Bristol-Myers Squibb Co. & Pfizer, Inc.

S. Connolly Disclosure: Received research grants,  
lecture and consulting fees from sponsors

# AF Patients Unsuitable for VKA

- There is a high risk of stroke in AF patients
- Vitamin K antagonist (VKA) therapy is effective against stroke, but it is considered unsuitable for up to 50% of patients
  - Difficult to control INR
  - Bleeding on VKA
- There is a need for an effective, safe and easy-to-use antithrombotic therapy for AF patients, unsuitable for VKA

# AVERROES Design

36 countries, 522 centres

AF and  $\geq 1$  risk factor, and demonstrated or expected unsuitable for VKA

Apixaban 5 mg BID

2.5 mg BID in selected patients

R

5,600 patients

Double-Blind

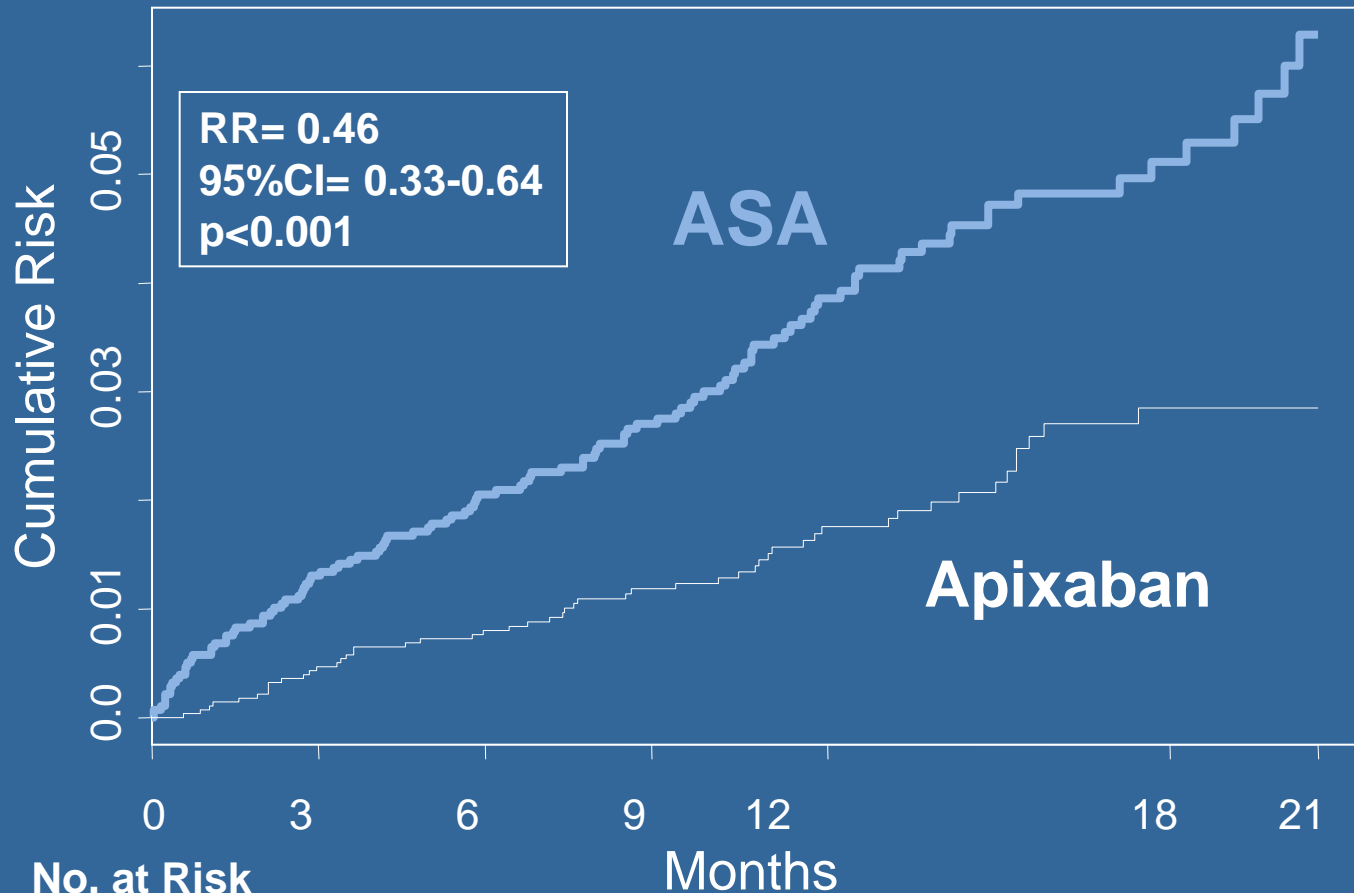
ASA (81-324 mg/d)

Primary Outcome: Stroke or Systemic Embolic Event (SEE)

# Baseline Characteristics

Characteristic	Apixaban	ASA
Randomized	2809	2791
Age (mean and SD)	70 ±10 yrs	70 ±10 yrs
Male	59%	58%
CHADS2 score (mean and SD)	2.1 ± 1.1	2.1± 1.1
0-1	36%	37%
2	37%	34%
3+	27%	29%
Prior stroke/TIA	14%	13%
Diabetes	19%	20%
Hypertension	86%	87%
CHF	40%	38%
Baseline ASA	76%	74%
Unsuitable for VKA		
VKA used and discontinued	39%	40%
VKA expected unsuitable	61%	60%

# Stroke or Systemic Embolic Event



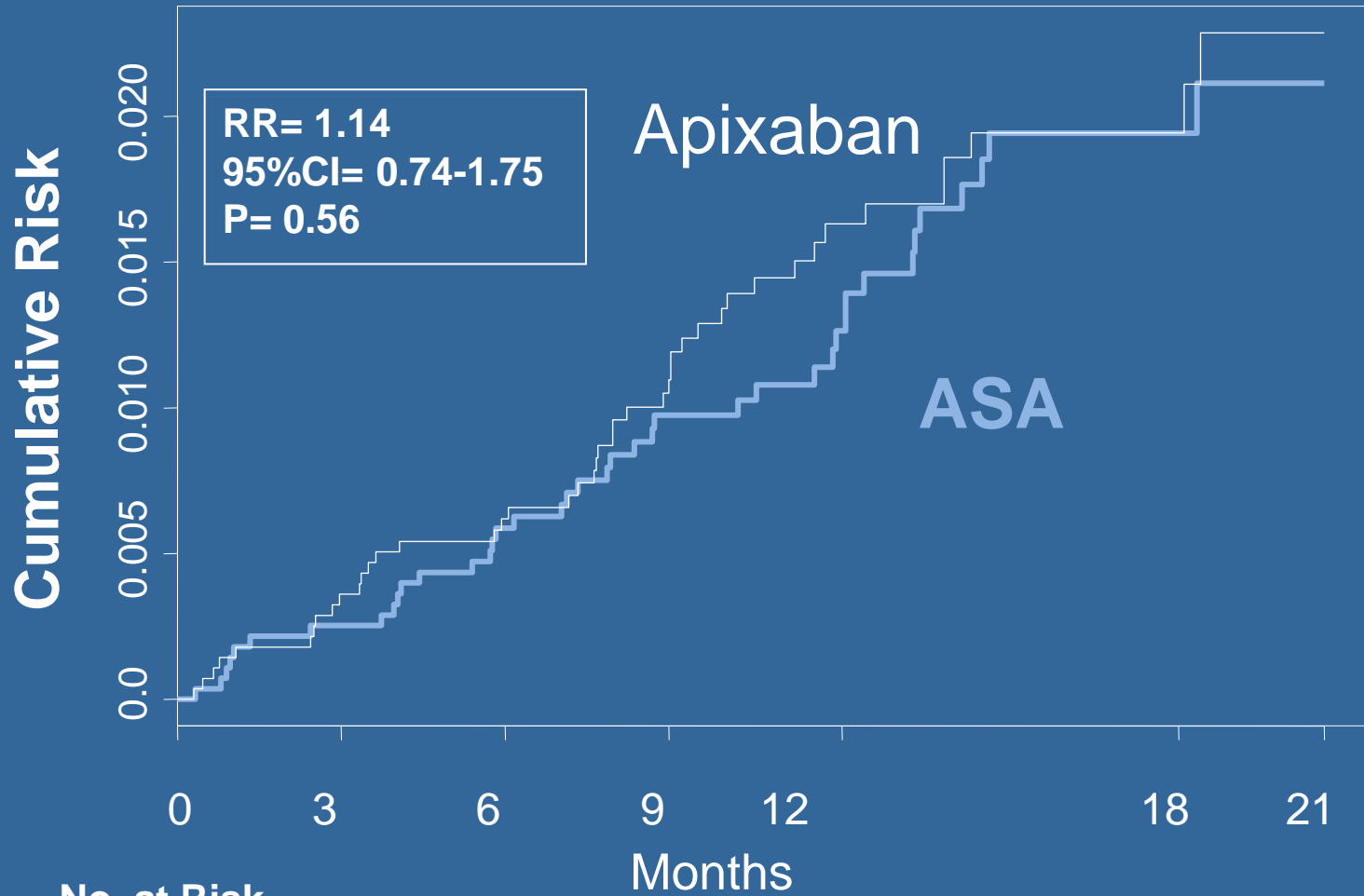
	0	3	6	9	12	18	21
<b>No. at Risk</b>							
ASA	2791	2720	2541	2124	1541	626	329
Apix	2809	2761	2567	2127	1523	617	353

preliminary Results

# Secondary and Other Efficacy Outcomes

Outcome	Apixaban		ASA		Apixaban vs. ASA		
	events	Annual rate	events	Annual rate	RR	95% CI	P
<b>Stroke, SEE,MI, or Vasc Death</b>	<b>129</b>	<b>4.1</b>	<b>193</b>	<b>6.2</b>	<b>0.66</b>	<b>0.53-0.83</b>	<b>&lt;0.001</b>
MI	22	0.7	26	0.8	0.85	0.48-1.50	0.57
Vasc Death	81	2.5	94	2.9	0.86	0.64-1.16	0.33
CV Hospitaliz.	346	11.8	432	14.9	0.79	0.68-0.91	<0.001
Total Death	110	3.4	139	4.4	0.79	0.62-1.02	0.07

# Major Bleeding



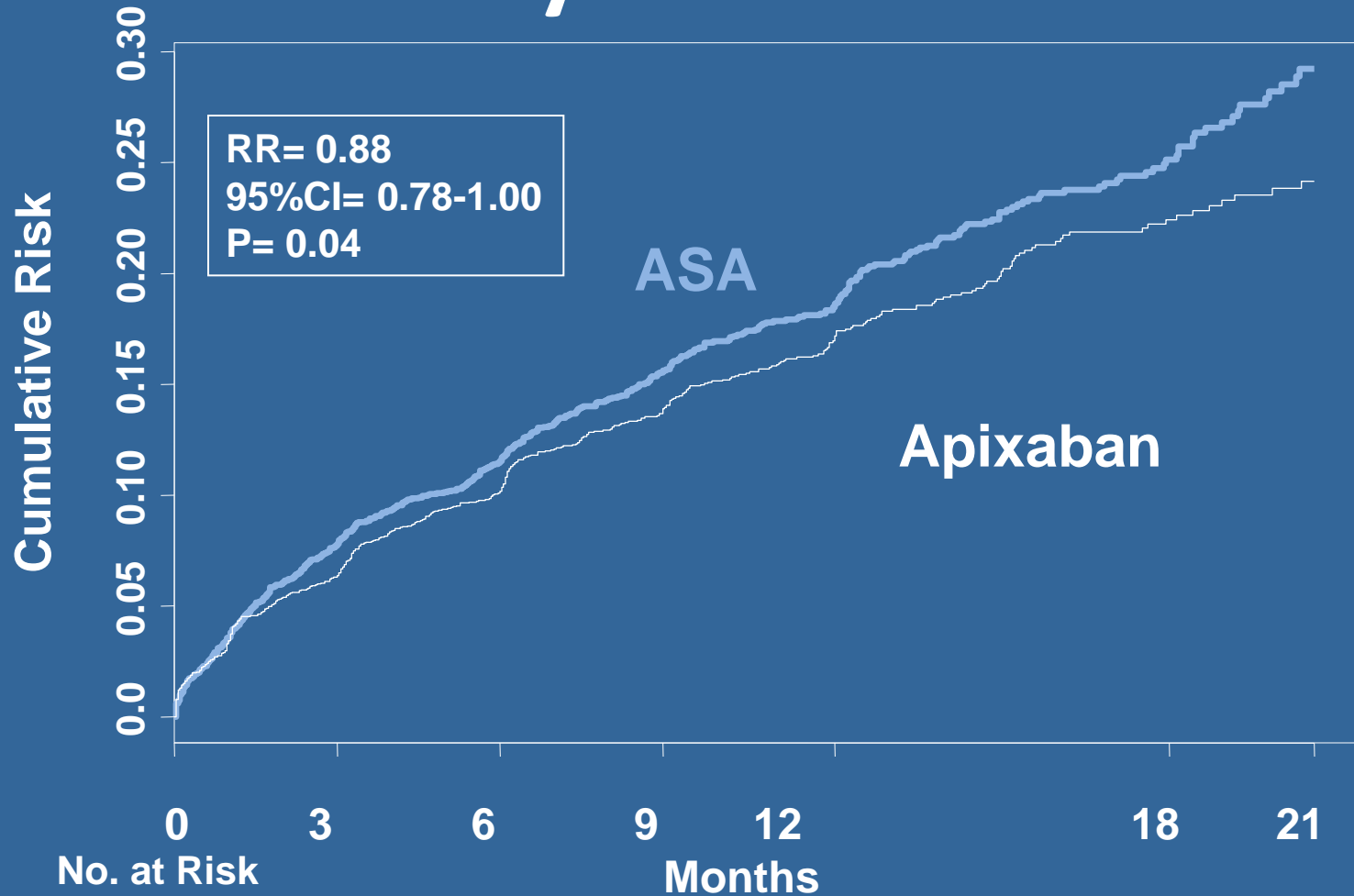
	No. at Risk						
	0	3	6	9	12	18	21
ASA	2791	2744	2572	2152	1570	642	340
Apix	2809	2763	2567	2123	1521	622	357

preliminary Results

# Bleeding

Outcome	Apixaban		ASA		Apixaban vs. ASA		
	events	Annual rate	events	Annual rate	RR	95% CI	P
<b>Major</b>	<b>44</b>	<b>1.4</b>	<b>39</b>	<b>1.2</b>	<b>1.14</b>	<b>0.74-1.75</b>	<b>0.56</b>
<b>Clinically Rel. Non-major</b>	<b>95</b>	<b>3.0</b>	<b>81</b>	<b>2.6</b>	<b>1.18</b>	<b>0.88-1.58</b>	<b>0.28</b>
<b>Minor</b>	<b>159</b>	<b>5.2</b>	<b>126</b>	<b>4.1</b>	<b>1.27</b>	<b>1.01-1.61</b>	<b>0.04</b>
<b>Fatal</b>	<b>5</b>	<b>0.1</b>	<b>6</b>	<b>0.1</b>	<b>0.84</b>	<b>0.26-2.75</b>	<b>0.77</b>
<b>Intra-cranial</b>	<b>13</b>	<b>0.4</b>	<b>12</b>	<b>0.3</b>	<b>1.09</b>	<b>0.50-2.39</b>	<b>0.83</b>

# Permanent Discontinuation of Study Medication



	0	3	6	9	12	18	21
ASA	2791	2567	2325	1906	1365	534	266
Apix	2809	2624	2356	1909	1328	521	299

preliminary Results

# 1000 Patients Treated with Apixaban for one year, instead of ASA

- Expect to Prevent
  - 18 strokes, mostly larger
  - 10 deaths\*
  - 31 cardiovascular hospitalizations
  
- At a cost of
  - 2 major bleeds\*

\* Statistically Non-significant