

**Rivaroxaban – an oral, direct Factor Xa inhibitor –  
versus enoxaparin for thromboprophylaxis after total  
knee replacement**

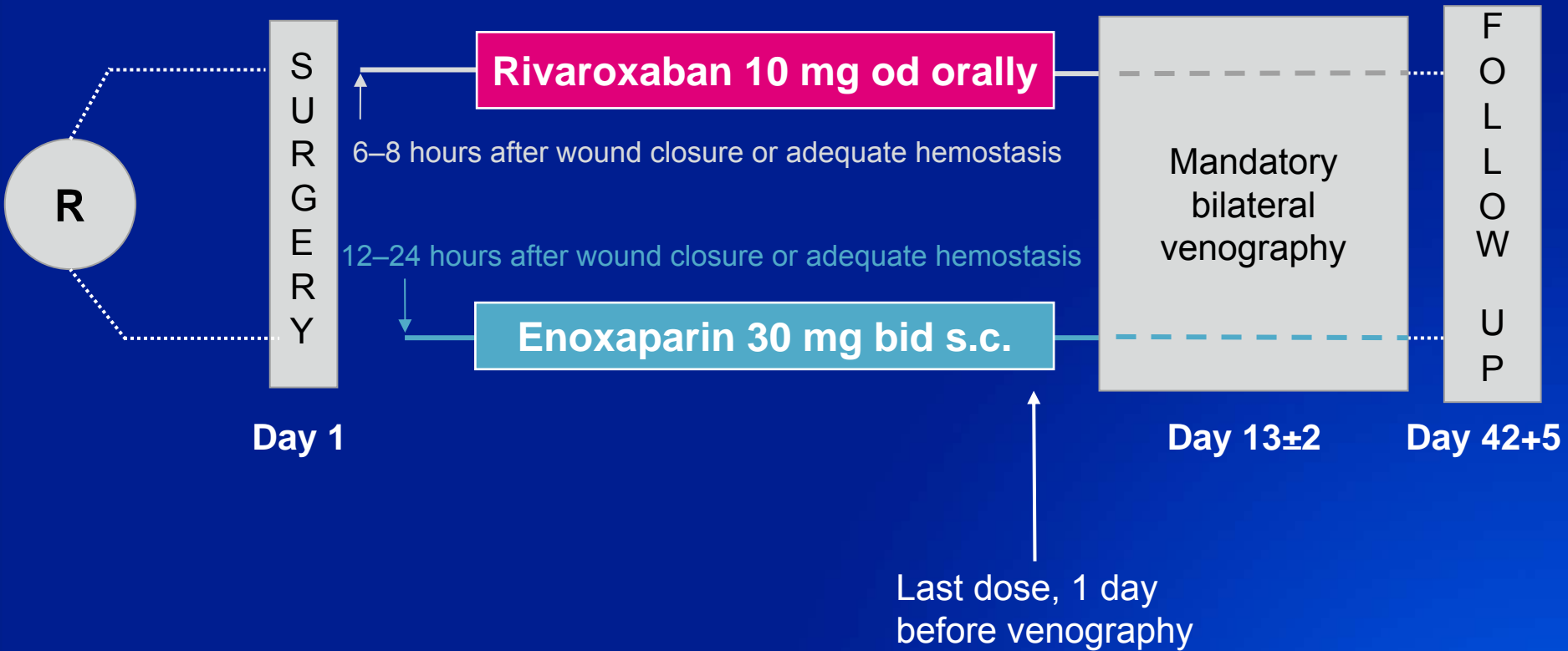
**RECORD4**

Alexander GG Turpie

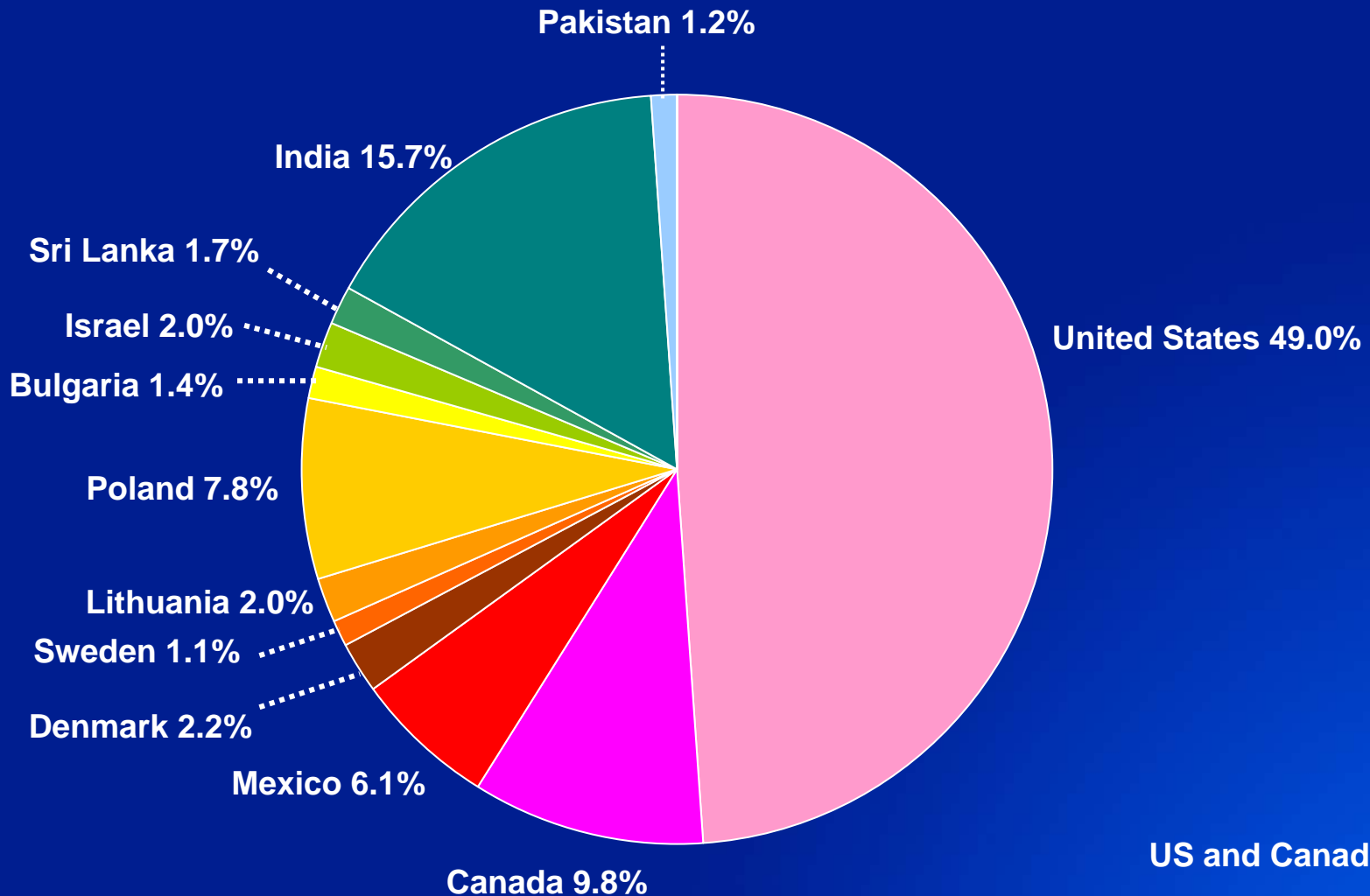
On behalf of Kenneth A Bauer, Scott D Berkowitz, Fred D  
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Fisher and the RECORD4 Study Investigators

# RECORD4: VTE prevention after total knee replacement

Double blind

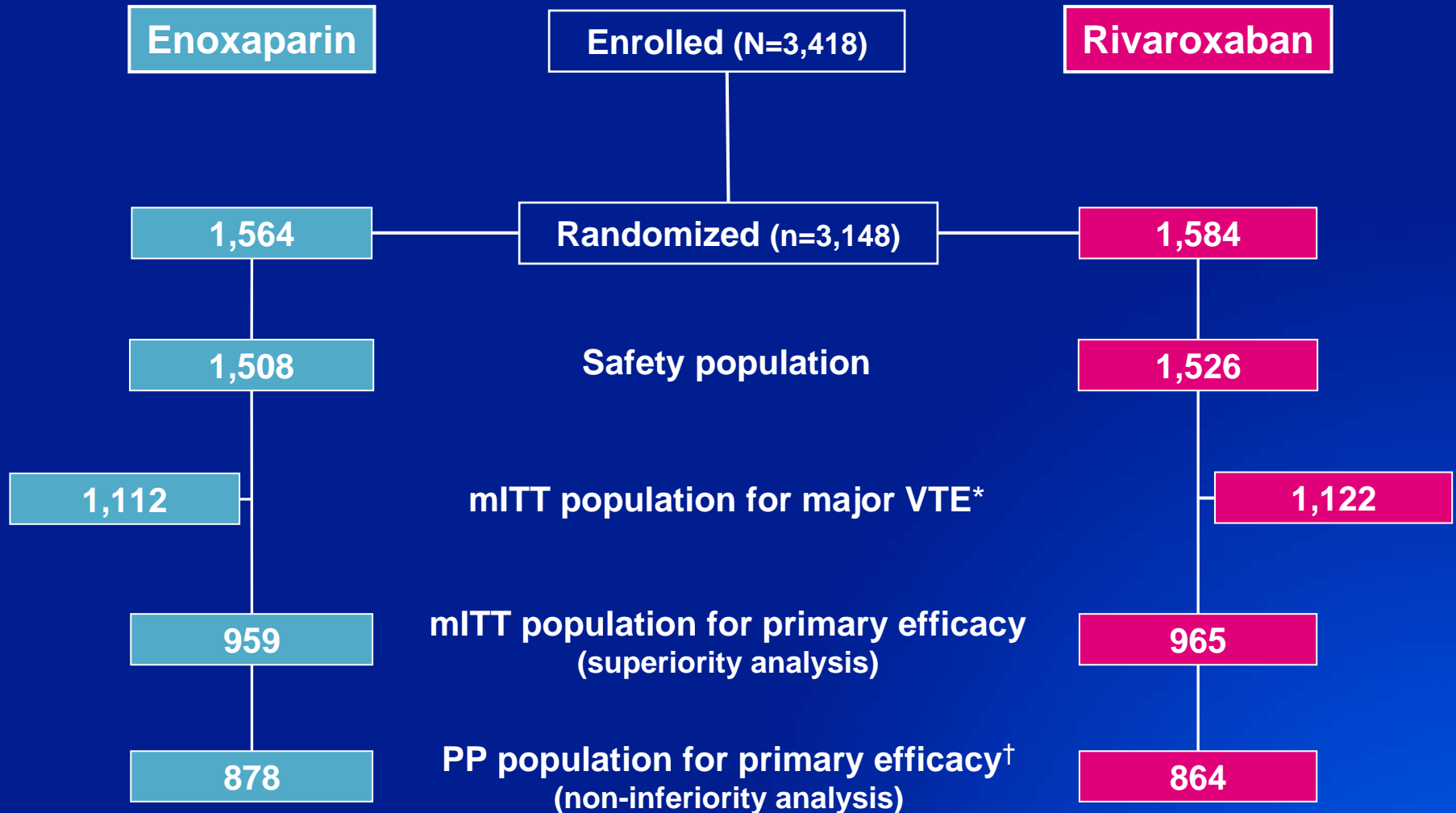


# Enrolment: 131 sites worldwide



US and Canada = 58.8%

# Study flow



\*Patients may be valid for major VTE analysis if only proximal veins were assessed

†Patients could have more than one protocol violation

# Patient demographics

	Enoxaparin 30 mg twice daily (n=1,508)		Rivaroxaban 10 mg once daily (n=1,526)	
Female, n %	967	<b>64.1%</b>	1,007	<b>66.0%</b>
Age*, years (range)	64.7	(24–89)	64.4	(21–87)
Weight*, kg (range)	84.4	(35–171.5)	84.7	(38–190)
Body mass index*, kg/m <sup>2</sup> (range)	30.7	(13.7–62.4)	30.9	(17.9–74.2)
Race, n %				
– Caucasian	1,032	<b>68.4%</b>	1,008	<b>66.1%</b>
– Black	65	<b>4.3%</b>	88	<b>5.8%</b>
– Asian	289	<b>19.2%</b>	289	<b>18.9%</b>
– Hispanic	116	<b>7.7%</b>	137	<b>9.0%</b>
– American Indian	5	<b>0.3%</b>	1	<b>0.1%</b>
– Other/data missing	2	<b>0.1%</b>	3	<b>0.2%</b>

\*Mean values

# Efficacy endpoints

## Primary

- ▶ Total VTE: any DVT, non-fatal PE and all-cause mortality up to day 13±4

## Secondary

- ▶ Major VTE: proximal DVT, non-fatal PE and VTE-related death
- ▶ DVT: any, proximal and distal
- ▶ Symptomatic VTE

# Safety endpoints

## Main

- ▶ Major bleeding starting after the first blinded dose and up to 2 days after last dose
  - Bleeding that was fatal, into a critical organ, or required re-operation
  - Extra-surgical-site bleeding associated with a drop in hemoglobin  $\geq 2$  g/dl or requiring transfusion of  $\geq 2$  units blood

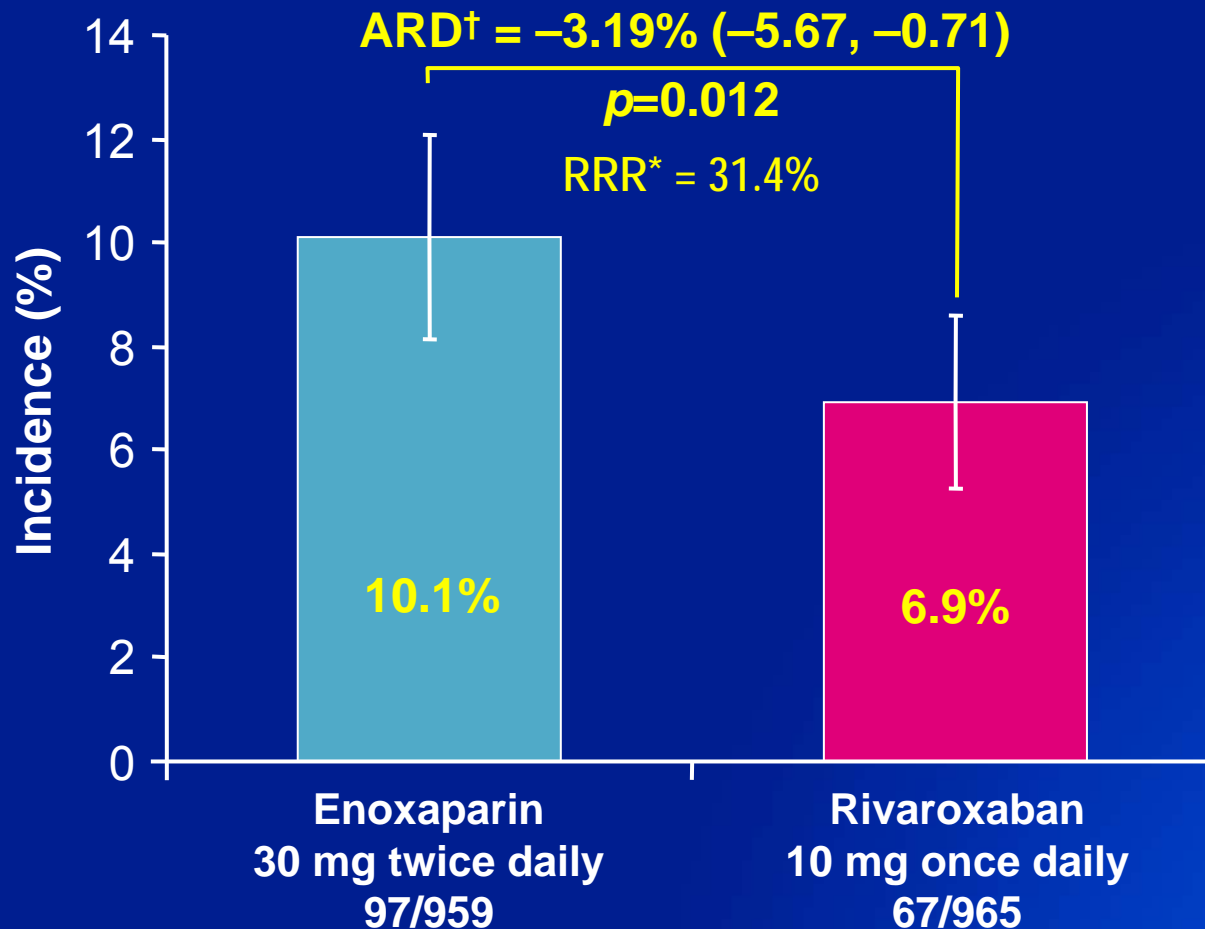
## Other

- ▶ Any bleeding on treatment\*
- ▶ Non-major bleeding\*
- ▶ Hemorrhagic wound complications\*
- ▶ Cardiovascular adverse events
- ▶ Liver enzyme levels

All endpoints were adjudicated centrally by independent, blinded committees

\*Up to 2 days after last dose of study medication

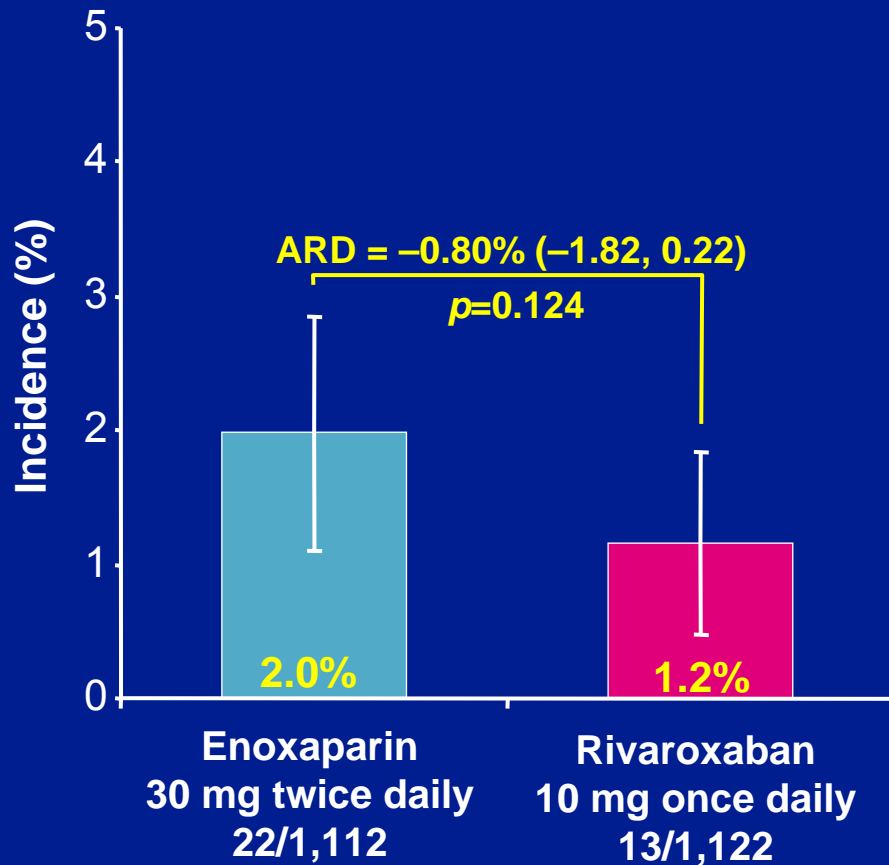
# Primary efficacy endpoint: total VTE



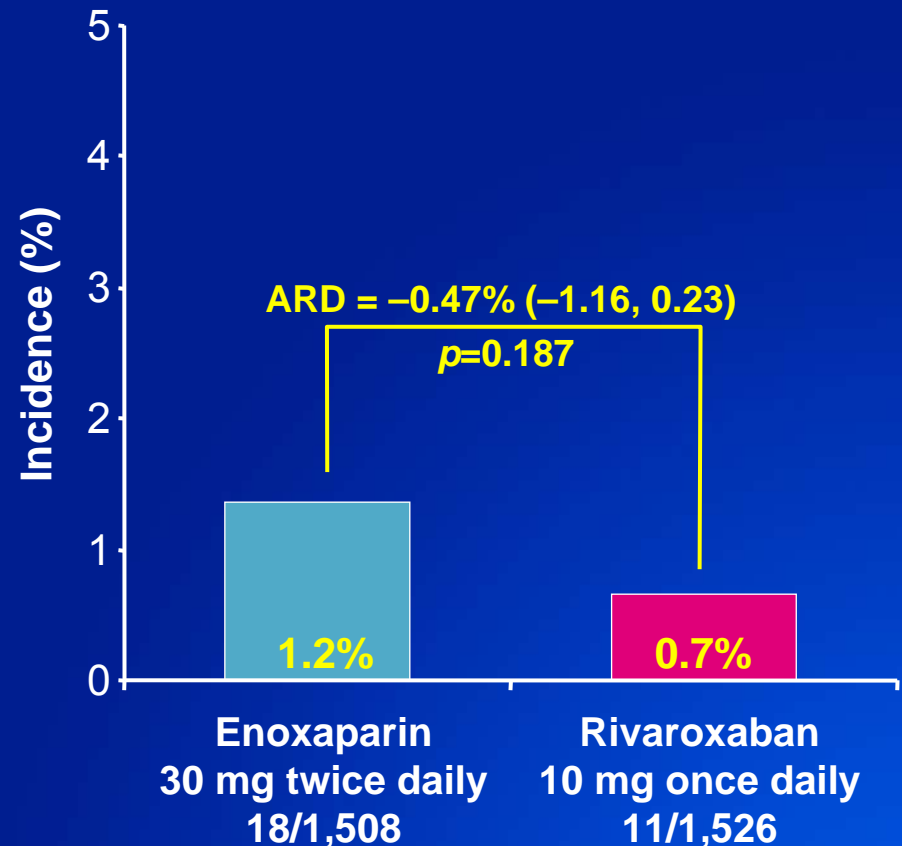
\*Relative risk reduction based on raw incidences; †absolute weighted risk difference (with 95% CI); mITT population, n=1,924

# Secondary efficacy endpoints

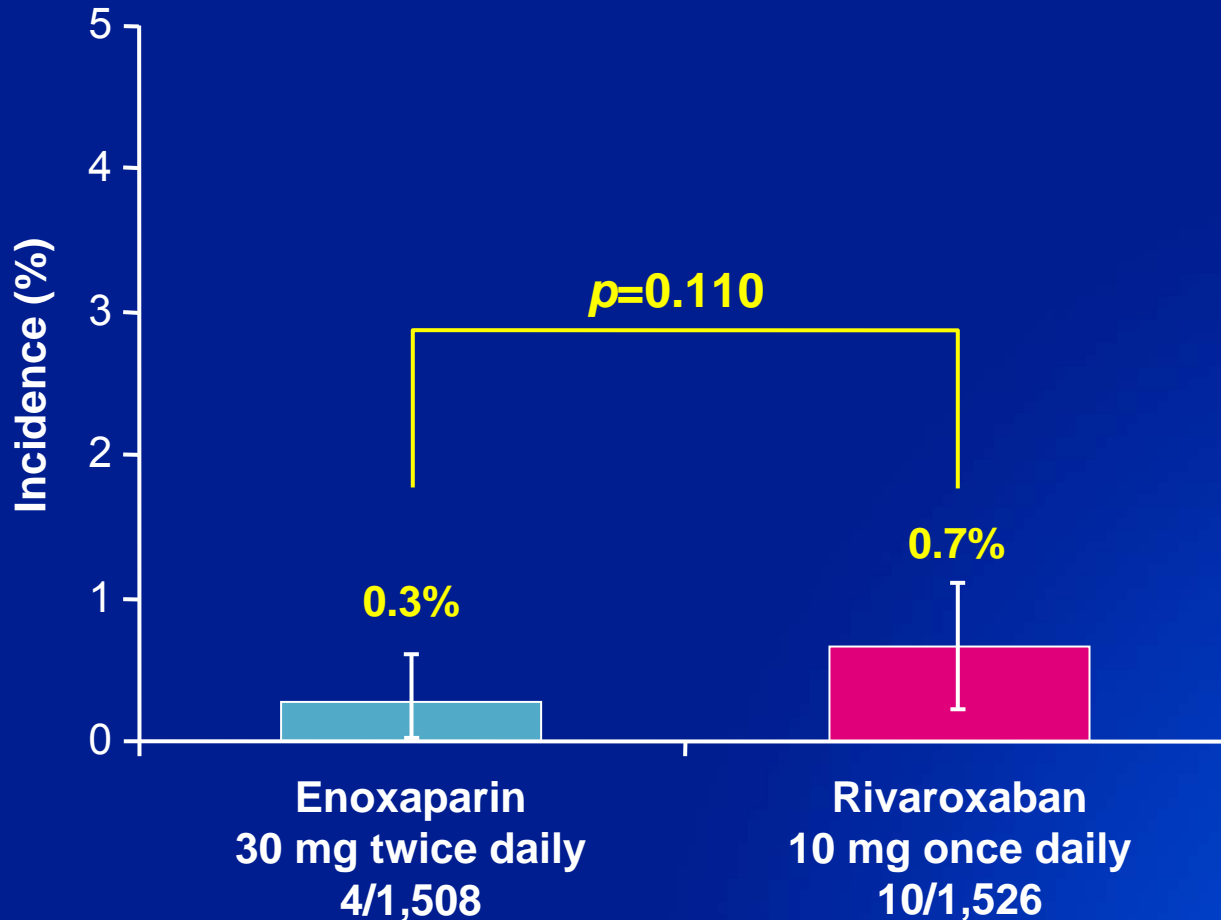
## Major VTE



## Symptomatic VTE



# Major bleeding



# Safety: components of bleeding

n %	Enoxaparin 30 mg twice daily (n=1,508)		Rivaroxaban 10 mg once daily (n=1,526)	
Any bleeding	142	<b>9.4%</b>	160	<b>10.5%</b>
Major bleeding	4	<b>0.3%</b>	10	<b>0.7%</b>
Fatal	0		1*	
Critical† (intraspinal, intracranial, retroperitoneal)	2		1	
Leading to fall in hemoglobin/transfusion	0		4	
Leading to re-operation	2		5	
Non-major bleeding	138	<b>9.2%</b>	155	<b>10.2%</b>
Clinically relevant non-major bleeding	30	<b>2.0%</b>	39	<b>2.6%</b>
Other non-major bleeding	112	<b>7.4%</b>	124	<b>8.1%</b>

\*1 patient had fatal post-operative upper GI bleed and a fall in hemoglobin leading to transfusion

# Adverse events

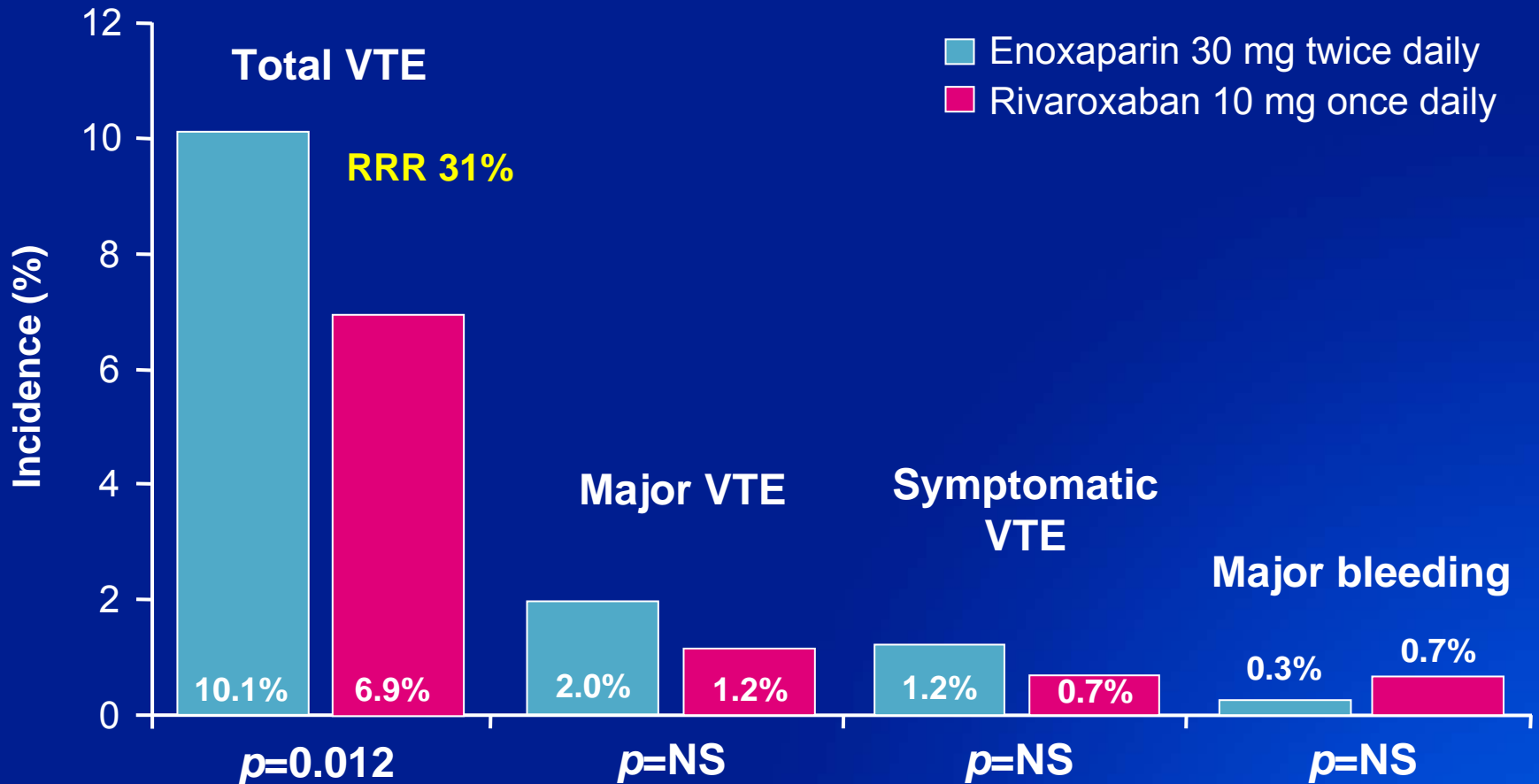
n %	Enoxaparin 30 mg twice daily (n=1,508)		Rivaroxaban 10 mg once daily (n=1,526)	
Any adverse event	1,312	<b>87.0%</b>	1,319	<b>86.4%</b>
On treatment	1,216	<b>80.6%</b>	1,222	<b>80.1%</b>
During follow-up	239	<b>15.8%</b>	244	<b>16.0%</b>
Cardiovascular adverse events (adjudicated)	11	<b>0.7%</b>	7	<b>0.5%</b>
On treatment	8	<b>0.5%</b>	2	<b>0.1%</b>
During follow-up*	3	<b>0.2%</b>	5	<b>0.3%</b>
Any post-operative wound-related infection	6	<b>0.4%</b>	6	<b>0.4%</b>
On treatment	3	<b>0.2%</b>	4	<b>0.3%</b>
Death	6	<b>0.4%</b>	6	<b>0.4%</b>

\*Events occurring more than 1 day after the last intake of study drug during follow-up; safety population, n=3,034

# Liver function tests: on-treatment elevations

n/N %	Enoxaparin 30 mg twice daily (n=1,508)	Rivaroxaban 10 mg once daily (n=1,526)
ALT >3× ULN	38/1,451 <b>2.6%</b>	19/1,470 <b>1.3%</b>
ALT >5× ULN	15/1,460 <b>1.0%</b>	5/1,478 <b>0.3%</b>
ALT >10× ULN	2/1,463 <b>0.1%</b>	1/1,480 <b>0.1%</b>
ALT >3× ULN + TB >2× ULN	3/1,464 <b>0.2%</b>	1/1,481 <b>0.1%</b>

# RECORD4: summary



# RECORD4: conclusions

## Rivaroxaban demonstrated:

- ▶ Superior efficacy for the primary endpoint (total VTE)
- ▶ Similar safety profile to enoxaparin
  - No statistically significant difference in major bleeding
  - Cardiovascular adverse events low and balanced between groups
  - No difference in the frequency of elevated hepatic enzymes or bilirubin