101. Vorapaxar vs. Placebo in Reducing Ischemic Events and Death Among Patients With Acute Coronary Syndrome: A Meta-Analysis

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Body

Background: Despite new treatment strategies for acute coronary syndrome (ACS), mortality and morbidity rates remain high. Newly developed drugs such as Vorapaxar should be assessed for efficacy and safety.

Vorapaxar is an orally available selective antagonist of the platelet protease-activated receptor-1. Results of clinical trials that evaluate its efficacy and safety in patients with coronary artery disease and/or ACS, have been inconsistent, hence a meta-analysis is warranted.

Methods: Randomized controlled trials evaluating the efficacy and safety of vorapaxar vs. standard therapy among patients with ACS were included. Primary efficacy outcome was all-cause death. Secondary efficacy outcomes were a composite of myocardial infarction, stroke, recurrent ischemia, or coronary revascularization - Major Adverse Cardiovascular Events (MACE). Primary safety outcome was TIMI major and minor bleeding.

Results: The meta-analysis of three randomized controlled trials encompassed a total of 30,840 patients.

Primary Outcome. Vorapaxar was associated with an insignificant 1% relative risk reduction (RRR) in death compared with controls (CI 0.88-1.12; p = 0.9).

Secondary Outcome. Vorapaxar showed a significant 10% RRR in MACE (CI 0.94-0.96; p = 0.0009), and a significant 16% RRR in the incidence of myocardial infarction (CI 0.78-0.91, p = <0.0001).

Safety Outcome. There is a statistically significant 1.6x increased risk for TIMI major or minor bleeding in the vorapaxar group (CI 1.37-1.77, p < 0.00001).

Conclusion: The addition of vorapaxar to standard therapy for ACS does not reduce all-cause death, but significantly reduces the risk of myocardial infarction, stroke, recurrent ischemia with rehospitalization, and urgent coronary revascularization. However, the addition of vorapaxar is associated with a more significant risk for bleeding.

Figure 1. Forrest plot for death

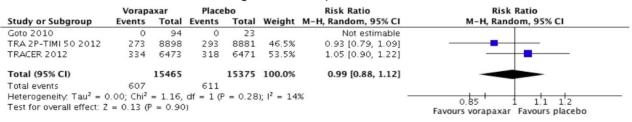


Figure 2. Forrest plot for major adverse cardiovascular events

Vorapaxar Placebo Risk Ratio Risk Ratio Study or Subgroup Events Total Events Total Weight M-H, Random, 95% CI M-H, Random, 95%		
Study or Subgroup Events Total Events Total Weight M-H, Random, 95% CI M-H, Random, 95% S	Risk Ratio M-H, Random, 95% CI	
TRA 2P-TIMI 50 2012 765 8898 874 8881 47.6% 0.87 [0.80, 0.96]		
TRACER 2012 823 6473 895 6471 52.4% 0.92 [0.84, 1.00]		
Total (95% Cl) 15371 15352 100.0% 0.90 [0.84, 0.96]		
Total events 1588 1769		
Heterogeneity: Tau ² = 0.00; Chi ² = 0.61, df = 1 (P = 0.43); $l^2 = 0\%$	+	
Test for overall effect: Z = 3.33 (P = 0.0009) Favours Vorapaxar Favours V	Placebo	

Figure 3. Forrest plot for myocardial infarction

	Vorapa	axar	Place	bo		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
Goto 2010	12	94	9	23	1.2%	0.33 [0.16, 0.68]	
TRA 2P-TIMI 50 2012	433	8898	541	8881	43.2%	0.80 [0.71, 0.90]	
TRACER 2012	621	6473	698	6471	55.7%	0.89 [0.80, 0.99]	•
Total (95% CI)		15465		15375	100.0%	0.84 [0.78, 0.91]	•
Total events	1066		1248				
Heterogeneity: $Chi^2 = 8$.21, df = 1	2(P = 0)	.02); 12 =	76%			0.01 0.1 1 10 100
Test for overall effect: Z	= 4.25 (F	° < 0.00	001)				Favours vorapaxar Favours placebo

Figure 4	. Forrest plot for	TIMI major/minor l	oleeding
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	Vorapaxar		Placebo		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Goto 2010	5	94	2	23	0.6%	0.61 [0.13, 2.96]	· · · · · · · · · · · · · · · · · · ·
TRA 2P-TIMI 50 2012	258	8898	162	8881	42.2%	1.59 [1.31, 1.93]	
TRACER 2012	337	6446	217	6441	57.1%	1.55 [1.31, 1.83]	
Total (95% CI)		15438		15345	100.0%	1.56 [1.37, 1.77]	•
Total events	600		381				
Heterogeneity: $Tau^2 = 0$	0.00; Chi ²	= 1.40,	df = 2 (1)	P = 0.50); $ ^2 = 0\%$		
Test for overall effect: $Z = 6.89$ (P < 0.00001)							Favours vorapaxar Favours placebo

Clinical Implications: decide whether or not to add vorapaxar to their treatment regimen for acute coronary syndrome.