



The TIMI Trials

PROVE IT-TIMI 22

OBJECTIVE: To compare the efficacy of atorvastatin vs. pravastatin and the clinical efficacy of the antibiotic gatifloxacin vs. placebo in a 2 x 2 factorial design among patients presenting with unstable angina or non-Q-wave myocardial infarction.

1. Cannon CP, McCabe CH, Belder R, Breen J, Braunwald E. Design of the Pravastatin or Atorvastatin Evaluation and Infection Therapy (PROVE IT)-TIMI 22 trial. *Am J Cardiol.* 2002;89:860-1.
2. Cannon CP, Braunwald E, McCabe CH, Rader DJ, Rouleau JL, Belder R, Joyal SV, Hill KA, Pfeffer MA, Skene AM. Intensive versus moderate lipid lowering with statins after acute coronary syndromes. *N Engl J Med* 2004;350:1495-1504.
3. Cannon CP, Braunwald E, McCabe CH, Grayston JT, Muhlstein B, Giugliano RP, Cairns R, Skene AM for the Pravastatin or Atorvastatin Evaluation and Infection Therapy – Thrombolysis in Myocardial Infarction (PROVE IT - TIMI) 22 Investigators. Antibiotic treatment of *Chlamydia pneumoniae* following acute coronary syndrome. *N Engl J Med* 2005;352:1646-54.
4. Giugliano RP, Cannon CP, Rader D, Grundy SM, McCabe CH, Braunwald E. Graded benefit of atorvastatin over pravastatin dependent upon baseline LDL. *Circulation* 2004;110:III-696.
5. Gibson CM, Sabatine MS, Murphy SA, Morrow DA, Wiviott SD, Smith S, McCabe CH, Cannon CP, Braunwald E. Association of intensive lipid lowering with reductions in target vessel revascularization (clinical restenosis) and non-target vessel revascularization (lesion progression): a PROVE-IT TIMI 22 substudy. *Circulation* 2004;110:III-696.
6. Sabatine MS, Wiviott SD, Morrow DA, McCabe CH, Cannon CP. High-dose atorvastatin associated with worse glycemic control: a PROVE-IT TIMI 22 substudy. *Circulation* 2004;110,(Suppl III):III-834.
7. Sabatine MS, Morrow DA, McCabe CH, Smith S, Meredith I, de Ferrari G, Gibson CM. Does intensive statin therapy reduce both urgent and elective coronary revascularization? Results from PROVE-IT TIMI 22. *Circulation* 2004;110,(Suppl III):III-696.
8. Wiviott SD, Cannon CP, Ray KK, Murphy SA, Darius H, Castaigne A, Velasco JA, McCabe CH, Gibson CM. Seasonal variations in lipid values in patients following acute coronary syndrome: PROVE IT-TIMI 22. *J Am Coll Cardiol* 2005; 45(3 Suppl A):394A.
9. Ray KK, Morrow DA, Murphy SA, McCabe CH, Gibson CM, Cannon CP. Baseline urinary albumin concentration predicts long-term cardiovascular risk in acute coronary syndrome patients: A PROVE IT-TIMI 22 substudy. *J Am Coll Cardiol* 2005; 45(3 Suppl A):195A.
10. Rose E, McCabe C, Cairns R, Cannon CP, Braunwald E. Dramatic benefit of intensive statin therapy in women: Results from PROVE IT – TIMI 22. *J Am Coll Cardiol* 2005;45:12A.
11. Ray KK, Cannon CP, Morrow DA, Cairns R, Braunwald E. Percutaneous coronary intervention for ACS is associated with a long-term reduction in CRP: An analysis from PROVE IT – TIMI 22. *Eur Heart J* 2005;26(abstr):39.
12. Ray KK, Cannon CP, Rader DJ, Cairns R, McCabe CH, Sacks FM, Braunwald E. Baseline ApoB predicts benefit of intensive statin therapy in patients with ACS: An analysis from PROVE IT-TIMI 22. *Eur Heart J* 2005;26(abstr):553.
13. Ahmed S, Cannon CP, McCabe CH, Murphy SA, Braunwald E. Acute coronary syndromes and diabetes mellitus: Does intensive lipid lowering work? *Eur Heart J* 2005;26(abstr):666.
14. Ray KK, Cannon CP, Morrow DA, Cairns R, McCabe CH, Ridker PM, Braunwald E. CRP is additive and independent of Apo B/A1 ratio in explaining the clinical benefits of atorvastatin 80 mg in ACS patients in PROVE IT – TIMI 22. *Circulation* 2005;112:II:483.
15. Wiviott SD, Cannon CP, Morrow DA, Ray KK, Pfeffer MA, Braunwald E. Can low-density lipoprotein be too low? The safety and efficacy of achieving very low low-density lipoprotein with intensive statin therapy: A PROVE IT-TIMI 22 Substudy. *J Am Coll Cardiol.* 2005;46(8):1411-6.
16. Ray KK, Cannon CP, Cairns R, Morrow DA, Rifai N, Kirtane AJ, McCabe CH, Skene AM, Gibson CM, Ridker PM, Braunwald E. Relationship between uncontrolled risk factors and C-reactive protein levels in

17. Wiviott SD, Cannon CP, Morrow DA, Ray KK, Pfeffer MA, Braunwald E. Can low-density lipoprotein be too low? The safety and efficacy of achieving very low low-density lipoprotein with intensive statin therapy: A PROVE IT – TIMI 22 substudy. *J Am Coll Cardiol* 2005;46:1411-6.
18. Ray KK, Cannon CP, McCabe CH, Cairns R, Tonkin AM, Sacks FM, Jackson G, Braunwald E for the PROVE IT-TIMI 22 Investigators. Early and late benefits of high-dose atorvastatin in patients with acute coronary syndromes. Results from the PROVE IT – TIMI 22 trial. *J Am Coll Cardiol* 2005;46:1405-10.
19. Ridker PM, Cannon CP, Morrow D, Rifai N, Rose LM, McCabe CH, Pfeffer MA, Braunwald E. C-reactive protein levels and outcomes after statin therapy. *N Engl J Med* 2005;352:20-8.
20. Ridker PM, Morrow D, Rose LM, Cannon CP, Braunwald E. Relative efficacy of atorvastatin 80 mg and pravastatin 40 mg in achieving the dual goals of low-density lipoprotein cholesterol <70 mg/dl and CRP < 2 mg/l: An analysis of the PROVE-IT TIMI 22 trial. *J Am Coll Cardiol* 2005;45:1644-8.
21. Ray KK, Cannon CP, Cairns R, Morrow DA, Rifai N, Kirtane AJ, McCabe CH, Skene AM, Gibson CM, Ridker PM, Braunwald E for the PROVE IT – TIMI 22 Investigators. Relationship between uncontrolled risk factors and c-reactive protein levels in patients receiving standard or intensive statin therapy for acute coronary syndromes in the PROVE IT - TIMI 22 trial. *J Am Coll Cardiol* 2005;46:1417-24.
22. Mega JL, Morrow DA, Cannon CP, Murphy S, Cairns R, Ridker PM, Braunwald E. Cholesterol, c-reactive protein, and cerebrovascular events following intensive and moderate statin therapy. *J Thromb Thrombolysis* 2006;22:71-6.
23. Ray KK, Bach RG, Cannon CP, Cairns R, Kirtane AJ, Wiviott SD, McCabe CH, Braunwald E, Gibson CM. Benefits of achieving the NCEP optional LDL-C goal among elderly patients with ACS. *Eur Heart J* 2006;27:2310-6.
24. O'Donoghue, M, Morrow DA, Sabatine MS, Murphy SA, McCabe CH, Cannon CP, Braunwald E. Lipoprotein-associated phospholipase A₂ and its association with cardiovascular outcomes in patients with acute coronary syndromes in the PROVE IT-TIMI 22 trial. *Circulation* 2006;113:1745-52.
25. Scirica BM, Morrow DA, Cannon CP, Ray KK, Sabatine MS, Jarolim P, Shui A, McCabe CH, Braunwald E for the PROVE IT-TIMI 22 investigators. Intensive statin therapy and the risk of hospitalization for heart failure after an acute coronary syndrome in the PROVE IT –TIMI 22 study. *J Am Coll Cardiol* 2006;47:2326-31.
26. Bonaca MP, Morrow DA, Sabatine MS, Kausik KR, Rifai N, Cannon CP. Elevated Levels of Placental Growth Factor (PlGF) and Long Term Risk in Patients in Acute Coronary Syndromes in PROVE IT-TIMI 22. *Circulation* 2006 114; 18 (Supp) II-649
27. Schweiger MJ, Giugliano RP, Lotfi A, Murphy SA, Cannon CP. High dose atorvastatin does not impact the efficacy of clopidogrel - A PROVE IT TIMI-22 analysis. *J Am Coll Cardiol* 2006;47(4):380A.
28. Ahmed S, Cannon CP, Murphy SA, Braunwald E. Acute coronary syndromes and diabetes: is intensive lipid lowering beneficial? Results of the PROVE IT-TIMI 22 Trial. *Eur Heart J*. 2006;27:2323-9.
29. Ray KK, Morrow DA, Sabatine MS, Shui A, Rifai N, Cannon CP, Braunwald E. Long-term prognostic value of neopterin: a novel marker of monocyte activation in patients with acute coronary syndrome. *Circulation*. 2007;115(24):3071-8.
30. Miller M, Cannon CP, Murphy SA, Qin J, Ray KK, Braunwald E. Impact of triglyceride levels beyond low-density lipoprotein cholesterol after acute coronary syndrome in the PROVE IT-TIMI 22 trial. *J Am Coll Cardiol*. 2008;51:724-30.
31. Lotfi A, Schweiger MJ, Giugliano GR, Murphy SA, Cannon CP. High-dose atorvastatin does not negatively influence clinical outcomes among clopidogrel treated acute coronary syndrome patients--a Pravastatin or Atorvastatin Evaluation and Infection Therapy-Thrombolysis in Myocardial Infarction 22 (PROVE IT-TIMI 22) analysis. *Am Heart J*. 2008;155:954-8.
32. Morrow DA, Wang Y, Croce K, Sakuma M, Sabatine MS, Gao H, Pradhan AD, Healy AM, Buros J, McCabe CH, Libby P, Cannon CP, Braunwald E, Simon DI. Myeloid-related protein 8/14 and the risk of cardiovascular death or myocardial infarction after an acute coronary syndrome in the Pravastatin or Atorvastatin Evaluation and Infection Therapy (PROVE IT – TIMI 22) trial. *Am Heart J* 2008;155:49-55.
33. Iakoubova OA, Sabatine MS, Rowland CM, Tong CH, Catanese JJ, Ranade K, Simonsen KL, Kirchgessner TG, Cannon CP, Devlin JJ, Braunwald E. Polymorphism in K1F6 gene and benefit from statins after acute coronary syndromes: Results from the PROVE IT - TIMI 22 study. *J Am Coll Cardiol* 2008;251:449-55.

34. Giraldez RR, Giugliano RP, Mohanavelu S, Murphy SA, McCabe CH, Cannon CP, Braunwald E. Baseline low-density lipoprotein cholesterol is an important predictor of the benefit of intensive lipid-lowering therapy: a PROVE IT-TIMI 22 (Pravastatin or Atorvastatin Evaluation and Infection Therapy-Thrombolysis In Myocardial Infarction 22) analysis. *J Am Coll Cardiol* 2008;52:914-20.