

Clinical trials of cholesterol lowering intervention for acute coronary syndrome in early initiation

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1 ezetimibe

Trial	Treatments	Patients	Trials design and methods
ezetimibe vs placebo (on top statins)			
IMPROVE-IT , 2014 [NCT00202878] n=9067/9077 follow-up: 5.68 years	10 mg/day of ezetimibe and 40 mg/day of simvastatin versus simvastatin 40 mg/day	subjects with stabilized high-risk acute coronary syndrome	Parallel groups double blind 39 countries

References

IMPROVE-IT, 2014:

Cannon CP, Blazing MA, Giugliano RP, McCagg A, White JA, Theroux P, Darius H, Lewis BS, Ophuis TO, Jukema JW, De Ferrari GM, Ruzyllo W, De Lucca P, Im K, Bohula EA, Reist C, Wiviott SD, Tereshakovec AM, Musliner TA, Braunwald E, Califf RM Ezetimibe Added to Statin Therapy after Acute Coronary Syndromes. N Engl J Med 2015;372:2387-97 [26039521]

2 statins

Trial	Treatments	Patients	Trials design and methods
atorvastatin vs placebo			
MIRACL , 2001 n=1538/1548 follow-up: 1 and 4 months	Atorvastatin, 80 mg (early initiation) versus Placebo	unstable angina or nonQ-wave acute MI	Parallel groups Double blind Europe, North America, South Africa, and Australasia
fluvastatin vs placebo			
LIPS (sub groups) , 2002 n=417/407 follow-up: 1, 4, and 6 months	Fluvastatin, 80 mg versus Placebo	patients with unstable angina and successful first percutaneous coronary intervention	Parallel groups double blind Europe, Canada, and Brazil
FLORIDA , 2002 n=265/275 follow-up: 1, 4, and 6 months	Fluvastatin, 80 mg (early initiation) versus Placebo	patients with an AMI and total cholesterol of <6.5 mmol.l	Parallel groups double blind The Netherlands

continued...

Trial	Treatments	Patients	Trials design and methods
Czech trial <i>ongoing</i> [NCT00171275] n=NA follow-up: 52 weeks	fluvastatin versus placebo	-	Parallel groups double blind
pravastatin vs placebo			
LAMIL , 1997 n=36/33 follow-up: 1 and 3 months	Pravastatin, 10-20 mg (starting at D3) versus Placebo	patients suffering an acute myocardial infarction	Parallel groups double blind Belgium
RECIFE , 1999 n=30/30 follow-up: 1.5 months	Pravastatin, 40 mg versus Placebo	Patients with acute myocardial infarction or unstable angina and total cholesterol levels at admission ≥ 5.2 mmol/L or LDL ≥ 3.4 mmol/L	Parallel groups double blind Canada
PAIS , 2001 n=50/49 follow-up: 1 and 3 months	Pravastatin, 40 mg (initiated within 48 hours of hospital admission) versus Placebo	patients with acute coronary syndromes	Parallel groups double blind The Netherlands
PACT , 2004 n=1710/1698 follow-up: 1 months	Pravastatin, 20-40 mg within 24 hours of the onset of symptoms in versus Placebo	patients with unstable angina, non-ST-segment elevation myocardial infarction, or ST-segment elevation myocardial infarction within 24 hours of the onset of symptoms	Parallel groups double blind Australia
simvastatin vs placebo			
A to Z , 2004 n=2265/2232 follow-up: 4 months	Simvastatin, 40-80 mg early initiation versus Placebo	patient with an acute coronary syndrome (ACS)	Parallel groups Double aveugle 41 countries
atorvastatin vs usual care			
Colivicchi , 2002 n=40/41 follow-up: 1, 3, and 6 months	Atorvastatin, 80 mg daily early initiation versus Usual care	unstable angina pectoris or non-Q-wave myocardial infarction	Parallel groups open Italy
ESTABLISH , 2004 n=35/35 follow-up: 1, 4, and 6 months	Atorvastatin, 20 mg early initiation versus Usual care	patients with ACS undergoing emergency coronary angiography and percutaneous coronary intervention	Parallel groups open Japan
pravastatin vs usual care			
L-CAD , 2000 n=70/56 follow-up: 1, 4, and 6 months	Pravastatin, 20-40 mg (strating on average at D6) versus Usual care	patients with acute coronary syndrome	Parallel groups open Germany
PTT , 2002 n=79/85 follow-up: 1 and 6 months	Pravastatin, 40 mg versus Usual care	patients who underwent coronary balloon angioplasty of the infarct-related artery during the first month of acute myocardial infarction	Parallel groups open Turkey

continued...

Trial	Treatments	Patients	Trials design and methods
pitavastatin vs atorvastatin			
JAPAN ACS , 2009 [NCT00242944] n=307 follow-up: 8-12 months	pitavastatin 4 mg daily versus atorvastatin 20mg daily	patients with acute coronary syndrome undergoing IVUS-guided percutaneous coronary intervention	Parallel groups open Japan
atorvastatin vs pravastatin			
PROVE IT - TIMI 22 , 2004 n=2099/2063 follow-up: 24 mo (18-36 mo)	80 mg of atorvastatin daily (intensive therapy). versus 40 mg of pravastatin daily (standard therapy)	patients who had been hospitalized for an acute coronary syndrome within the preceding 10 days	Parallel groups double blind UK, US, AUstralia, Italy, France, Germany, Spain, Canada

References

MIRACL, 2001:

Schwartz GG, Olsson AG, Ezekowitz MD, Ganz P, Oliver MF, Waters D, Zeiher A, Chaitman BR, Leslie S, Stern T Effects of atorvastatin on early recurrent ischemic events in acute coronary syndromes: the MIRACL study: a randomized controlled trial. *JAMA* 2001 Apr 4;285:1711-8 [[11277825](#)]

LIPS (sub groups), 2002:

Serruys PW, de Feyter P, Macaya C, Kokott N, Puel J, Vrolix M, Branzi A, Bertolami MC, Jackson G, Strauss B, Meier B Fluvastatin for prevention of cardiac events following successful first percutaneous coronary intervention: a randomized controlled trial. *JAMA* 2002 Jun 26;287:3215-22 [[12076217](#)]

FLORIDA, 2002:

Liem AH, van Boven AJ, Veeger NJ, Withagen AJ, Robles de Medina RM, Tijssen JG, van Veldhuisen DJ Effect of fluvastatin on ischaemia following acute myocardial infarction: a randomized trial. *Eur Heart J* 2002;23:1931-7 [[12473255](#)]

Czech trial, :

LAMIL, 1997:

Kesteloot H, Claeys G, Blanckaert N, Lesaffre E Time course of serum lipids and apolipoproteins after acute myocardial infarction: modification by pravastatin. *Acta Cardiol* 1997;52:107-16 [[9187418](#)]

RECIFE, 1999:

Dupuis J, Tardif JC, Cernacek P, Throux P Cholesterol reduction rapidly improves endothelial function after acute coronary syndromes. The RECIFE (reduction of cholesterol in ischemia and function of the endothelium) trial. *Circulation* 1999;99:3227-33 [[10385495](#)]

PAIS, 2001:

Den Hartog FR, Van Kalmthout PM, Van Loenhout TT, Schaafsma HJ, Rila H, Verheugt FW Pravastatin in acute ischaemic syndromes: results of a randomised placebo-controlled trial. *Int J Clin Pract* 2001;55:300-4 [[11452676](#)]

PACT, 2004:

Thompson PL, Meredith I, Amerena J, et al. Effect of pravastatin compared with placebo initiated within 24 hours of onset of acute myocardial infarction or unstable angina: the Pravastatin in Acute Coronary Treatment (PACT) trial *Am Heart J*. 2004;148:e2

Thompson PL, Meredith I, Amerena J, Campbell TJ, Sloman JG, Harris PJ Effect of pravastatin compared with placebo initiated within 24 hours of onset of acute myocardial infarction or unstable angina: the Pravastatin in Acute Coronary Treatment (PACT) trial. *Am Heart J* 2004;148:e2 [[15215811](#)]

A to Z, 2004:

de Lemos JA, Blazing MA, Wiviott SD, Lewis EF, Fox KA, White HD, Rouleau JL, Pedersen TR, Gardner LH, Mukherjee R, Ramsey KE, Palmisano J, Bilheimer DW, Pfeffer MA, Califf RM, Braunwald E Early intensive vs a delayed conservative simvastatin strategy in patients with acute coronary syndromes: phase Z of the A to Z trial. *JAMA* 2004 Sep 15;292:1307-16 [[15337732](#)]

Colivicchi, 2002:

Colivicchi F, Guido V, Tubaro M, Ammirati F, Montefoschi N, Varveri A, Santini M Effects of atorvastatin 80 mg daily early after onset of unstable angina pectoris or non-Q-wave myocardial infarction. *Am J Cardiol* 2002;90:872-4 [[12372577](#)]

ESTABLISH, 2004:

Okazaki S, Yokoyama T, Miyauchi K, Shimada K, Kurata T, Sato H, Daida H Early statin treatment in patients with acute coronary syndrome: demonstration of the beneficial effect on atherosclerotic lesions by serial volumetric intravascular ultrasound analysis during half a year after coronary event: the ESTABLISH Study. *Circulation* 2004;110:1061-8 [[15326073](#)]

L-CAD, 2000:

Arntz HR, Agrawal R, Wunderlich W, Schnitzer L, Stern R, Fischer F, Schultheiss HP Beneficial effects of pravastatin (+/-colestyramine/niacin) initiated immediately after a coronary event (the randomized Lipid-Coronary Artery Disease [L-CAD] Study). *Am J Cardiol* 2000;86:1293-8 [[11113401](#)]

PTT, 2002:

Kayikioglu M, Can L, Kltrsay H, Payzin S, Turkoglu C Early use of pravastatin in patients with acute myocardial infarction undergoing coronary angioplasty. *Acta Cardiol* 2002;57:295-302 [[12222700](#)]

JAPAN ACS, 2009:

Hiro T, Kimura T, Morimoto T, Miyauchi K, Nakagawa Y, Yamagishi M, Ozaki Y, Kimura K, Saito S, Yamaguchi T, Daida H, Matsuzaki M Effect of intensive statin therapy on regression of coronary atherosclerosis in patients with acute coronary syndrome: a multicenter randomized trial evaluated by volumetric intravascular ultrasound using pitavastatin versus atorvastatin (JAPAN-ACS [Japan assessment of pitavastatin and atorvastatin in acute coronary syndrome] study). *J Am Coll Cardiol* 2009 Jul 21;54:293-302 [[19608026](#)]
[10.1016/j.jacc.2009.04.033](https://doi.org/10.1016/j.jacc.2009.04.033)

PROVE IT - TIMI 22, 2004:

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 Apr 8;350:1495-504 [[15007110](#)]

Rouleau J Improved outcome after acute coronary syndromes with an intensive versus standard lipid-lowering regimen: results from the Pravastatin or Atorvastatin Evaluation and Infection Therapy-Thrombolysis in Myocardial Infarction 22 (PROVE IT-TIMI 22) trial. *Am J Med* 2005 Dec;118 Suppl 12A:28-35 [[16356805](#)]

Murphy SA, Cannon CP, Wiviott SD, de Lemos JA, Blazing MA, McCabe CH, Califf RM, Braunwald E Effect of intensive lipid-lowering therapy on mortality after acute coronary syndrome (a patient-level analysis of the Aggrastat to Zocor and Pravastatin or Atorvastatin Evaluation and Infection Therapy-Thrombolysis in Myocardial Infarction 22 trials). *Am J Cardiol* 2007 Oct 1;100:1047-51 [[17884359](#)]

Ray KK, Cannon CP, McCabe CH, Cairns R, Tonkin AM, Sacks FM, Jackson G, Braunwald E 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 Oct 18;46:1405-10 [[16226162](#)]

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 Sep 9;52:914-20 [[18772061](#)]

3 About TrialResults-center.org

TrialResults-center is an innovative knowledge database that collects the results of RCTs and provides dynamic interactive systematic reviews and meta-analysis in the field of all major heart and vessels diseases.

The TrialResults-center database provides a unique view of the treatment efficacy based on all data provided directly from clinical trial results, offering a valuable alternative to personal bibliographic search, published meta-analysis, etc. Furthermore, it would allow comparing easily the various concurrent therapeutic for the same clinical condition.

Rigorous meta-analysis method is used to populate TrialResults-center: widespread search of published and non published trials, study selection using pre-specified criteria, data extraction using standard form.

TrialResults-center is continually updated on a weekly basis. We continually search all new results (whatever their publication channel) and these news results are immediately added to the database with a maximum of 1 week.

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