Clinical trials of antithrombotics for percutaneous coronary intervention in PCI with stent placement

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1 6 months DAPT

Trial	Treatments	Patients	Trials design and methods
6-month dual antiplatelet therapy vs 12 months dual antiplatelet			
EXCELLENT , 2011 [NCT00698607] n=721/722 follow-up:	dual antiplatelet therapy for six months versus dual antiplatelet therapy for one year	patients with coronary artery disease	
12 months dual antiplatelet vs 6 months dual antiplatelet			
ISAR-SAFE , 2009 [NCT00661206] n=NA follow-up: 12 months	additional 6 month period of clopidogrel versus placebo	Patients on clopidogrel therapy at least 6 months after DES implantation, who do not require a reintervention	Parallel groups double blind

References

EXCELLENT, 2011:

Gwon HC, Hahn JY, Park KW, Song YB, Chae IH, Lim DS, Han KR, Choi JH, Choi SH, Kang HJ, Koo BK, Ahn T, Yoon JH, Jeong MH, Hong TJ, Chung WY, Choi YJ, Hur SH, Kwon HM, Jeon DW, Kim BO, Park SH, Lee NH, Jeon HK, Jang Y, Kim HS Six-month versus 12-month dual antiplatelet therapy after implantation of drug-eluting stents: the Efficacy of Xience/Promus Versus Cypher to Reduce Late Loss After Stenting (EXCELLENT) randomized, multicenter study. Circulation 2012;125:505-13 [22179532] 10.1161/CIRCULATIONAHA.111.059022

ISAR-SAFE, 2009:

Byrne RA, Schulz S, Mehilli J, Iijima R, Massberg S, Neumann FJ, ten Berg JM, Schmig A, Kastrati A Rationale and design of a randomized, double-blind, placebo-controlled trial of 6 versus 12 months clopidogrel therapy after implantation of a drug-eluting stent: The Intracoronary Stenting and Antithrombotic Regimen: Safety And EFficacy of 6 Months Dual Antiplatelet Therapy After Drug-Eluting Stenting (ISAR-SAFE) study. Am Heart J 2009 Apr;157:620-4.e2 [19332187] 10.1016/j.ahj.2008.12.019

2 antiplatelet drugs

Trial	Treatments	Patients	Trials design and methods
cilostazol vs aspirin			
Kunishima , 1997 n=30/40	Cilostazol 200 mg qD unspecified durationg qD versus Aspirin 81 mg qD	-	

continued...

Trial	Treatments	Patients	Trials design and methods
cilostazol + aspirin vs aspirin			
Sekiya , 1998 n=63/63	Cilostazol 200 mg qD x6mos Aspirin 81 mg qD versus Coumadin unspecified regimen Aspirin 81 mg qD	-	
ticlopidine + aspirin vs aspirin			
STARS (vs aspirin) , 1998 n=546/557 follow-up:	Ticlopidine 250 mg BID 4 wks Aspirin 325 mg qDDage/pj versus Aspirin 325 mg qD	-	
Hall , 1996 n=13/103	Ticlopidine 250 mg BID 1 mo Aspirin 325 mg qD 5 days versus Aspirin 325 mg qD	-	
ticlopidine + aspirin vs coumadin + aspirin			
STARS (vs coumadin+asp) , 1998 n=546/550 follow-up:	Ticlopidine 250 mg BID x4 wks Aspirin 325 mg qD versus Coumadin INR 22.5 x4 wks Aspirin 325 mg qDBID	-	
FANTASTIC , 1998 n=243/230	Ticlopidine 250 mg BID 6 wks Aspirin 100325 mg qD versus Coumadin INR 2.53.0 6 wks Aspirin 100325 mg qD/pj	-	
ISAR , 1996 n=257/260 follow-up:	Ticlopidine 250 mg BID 4 wks Aspirin 100 mg BIDage/pj versus Coumadin INR 3.54.5 4 wks Aspirin 100 mg BID	-	
MATTIS , 1998 n=177/173	Ticlopidine 250 mg BID 30 days Aspirin 250 mg qD versus Coumadin INR 2.53.0 x30 days Aspirin 250 mg qDg qD/pj	-	
Foussas , 2000 n=203/201	Ticlopidine 500mg qD 1 mo Aspirin 325 mg qD versus Coumadin INR 23 x4 wks Aspirin 325 mg qDg BID	-	
cilostazol + aspirin vs ticlopidine + aspirin			

continued...

Trial	Treatments	Patients	Trials design and methods
Kozuma , 2001 n=62/63	Cilostazol 200 mg qD x6 mos Aspirin 81162 mg qD versus Ticlopidine 200 mg qD x6 mos Aspirin 81162 mg qD	-	
Ochiai , 1999 n=25/25	Cilostazol 100 mg BID x6 mos Aspirin 81 mg TID versus Ticlopidine 100 mg BID x1 mo Aspirin 81 mg TID	-	
Park , 1999 n=247/243	Cilostazol 100 mg BID x6 mos Aspirin 200 mg qD versus Ticlopidine 250 mg BID x4 wks Aspirin 200 mg qD	-	
Yoon , 1999 n=147/149	Cilostazol 100 mg BID x30 days Aspirin 100 mg qD versus Ticlopidine 250 mg BID x30 days Aspirin 100 mg qD	-	
Kamishirado , 2002 n=65/65	Cilostazol 200 mg qD x6 mos Aspirin 81 mg qD versus Ticlopidine 200 mg qD x6 mos Aspirin 81 mg qD	-	
clopidogrel + aspirin vs ticlopidine + aspirin			
Mller , 2000 n=355/345	Clopidogrel 75 mg qD x4 wks Aspirin 100 mg qD versus Ticlopidine 250 mg BID x4 wks Aspirin 100 mg qD	-	
CLASSICS , 2000 n=345/340	Clopidogrel 300mg x1, 75 mg qD x4 wks Aspirin 325 mg qDyp ‘ versus Ticlopidine 250 mg BID x4 wks Aspirin 325 mg qD	-	
TOPPS , 2001 n=494/522	Clopidogrel 300 mg x1, unsp. Dose x2 wks Aspirin 325 mg qD versus Ticlopidine 500 mg x1, unsp. Dose x2 wks Aspirin 325 mg qD	-	
Piamsomboon , 2001 n=37/31	Clopidogrel 300 mg x1, 75 mg qD x4 wks Aspirin 300 mg BID x4 wks, 300 mg qD versus Ticlopidine 250 mg po BID x4 wks Aspirin 300 mg BID x4 wks, 300 mg qD	-	

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Kunishima T, Musha H, Eto F, Iwasaki T, Nagashima J, Masui Y, So T, Nakamura T, Oohama N, Murayama M A randomized trial of aspirin versus cilostazol therapy after successful coronary stent implantation. Clin Ther 1997;19:1058-66 [9385493]

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STARS (vs coumadin+asp), 1998:

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3 dual antiplatelet therapy

Trial	Treatments	Patients	Trials design and methods
Monitoring Adjusted Antiplatelet Treatment vs Common Antiplatelet Treatment			
ARTIC adjusted *ongoing* n=NA	-	-	
high-dose clopidogrel vs normal-dose clopidogrel			
GRAVITAS , 2011 [NCT00645918] n=1109/1105 follow-up: 6 months	High-dose clopidogrel (600-mg initial dose, 150 mg daily thereafter) versus regular clopidogrel dose	patients receiving drug-eluting stents with high residual platelet activity (PRU>=230) on the regular clopidogrel dose (platelet-function tests with the VerifyNow assay 12 to 24 hours after PCI)	Parallel groups open North America

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Collet JP, Cuisset T, Rang G, Cayla G, Elhadad S, Pouillot C, Henry P, Motreff P, Carri D, Boueri Z, Belle L, Van Belle E, Rousseau H, Aubry P, Monsgu J, Sabouret P, O'Connor SA, Abtan J, Kerneis M, Saint-Etienne C, Barthlmy O, Beygui F, Silvain J, M Bedside Monitoring to Adjust Antiplatelet Therapy for Coronary Stenting. N Engl J Med 2012 Nov 4;: [23121439] 10.1056/NEJMoa1209979

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4 prolonged dual antiplatelet therapy

Trial	Treatments	Patients	Trials design and methods
18 months dual antiplatelet vs 12 months dual antiplatelet			
ARTIC (extended dual antiplatelet) *ongoing* [NCT00827411] n=NA follow-up:	Pursuit of a dual oral antiplatelet therapy (aspirin and clopidogrel) beyond one year versus Interruption of clopidogrel therapy after one year	-	
prolonged dual antiplatelet therapy vs 12 months dual antiplatelet			
DES-LATE , 2010 [NCT00484926] n=1357/1344 follow-up: 19.2 mo	dual antiplatelet therapy (clopidogrel plus aspirin) versus aspirin alone	patients who had received drug eluting stents and had been free of major adverse cardiac or cerebrovascular events and major bleeding for a period of at least 12 months	Parallel groups open South Korea
OPTIMIZED *ongoing* n=NA	-	-	
DAPT *ongoing* [NCT00977938] n=20645 follow-up:	additional 18 months of thienopyridine treatment versus placebo	Subjects Undergoing Percutaneous Coronary Intervention With Either Drug-eluting Stent or Bare Metal Stent Placement for the Treatment of Coronary Artery Lesions	

References

ARTIC (extended dual antiplatelet), 0:

DES-LATE, 2010:

Park SJ, Park DW, Kim YH, Kang SJ, Lee SW, Lee CW, Han KH, Park SW, Yun SC, Lee SG, Rha SW, Seong IW, Jeong MH, Hur SH, Lee NH, Yoon J, Yang JY, Lee BK, Choi YJ, Chung WS, Lim DS, Cheong SS, Kim KS, Chae JK, Nah DY, Jeon DS, Seung KB, Jang JS, Park HS, Le Duration of Dual Antiplatelet Therapy after Implantation of Drug-Eluting Stents. N Engl J Med 2010 Mar 15;: [20231231] 10.1056/NEJMoa1001266

OPTIMIZED, :

DAPT, :

Mauri L, Kereiakes DJ, Yeh RW, Driscoll-Shempp P, Cutlip DE, Steg PG, Normand SL, Braunwald E, Wiviott SD, Cohen DJ, Holmes DR Jr, Krucoff MW, Hermiller J, Dauerman HL, Simon DI, Kandzari DE, Garratt KN, Lee DP, Pow TK, Lee PV, Rinaldi MJ, Massaro JM Twelve or 30 Months of Dual Antiplatelet Therapy after Drug-Eluting Stents. N Engl J Med 2014 Nov 16;: [25399658] 10.1056/NEJMoa1409312

5 prolonged dual antiplatelet therapyantiplatelet th

Trial	Treatments	Patients	Trials design and methods
prolonged dual antiplatelet therapy vs 12 months dual antiplatelet			

continued...

Trial	Treatments	Patients	Trials design and methods
DES-LATE , 2010 [NCT00484926] n=1357/1344 follow-up: 19.2 mo	dual antiplatelet therapy (clopidogrel plus aspirin) versus aspirin alone	patients who had received drug eluting stents and had been free of major adverse cardiac or cerebrovascular events and major bleeding for a period of at least 12 months	Parallel groups open South Korea
OPTIMIZED *ongoing* n=NA	-	-	
DAPT *ongoing* [NCT00977938] n=20645 follow-up:	additional 18 months of thienopyridine treatment versus placebo	Subjects Undergoing Percutaneous Coronary Intervention With Either Drug-eluting Stent or Bare Metal Stent Placement for the Treatment of Coronary Artery Lesions	

References

DES-LATE, 2010:

Park SJ, Park DW, Kim YH, Kang SJ, Lee SW, Lee CW, Han KH, Park SW, Yun SC, Lee SG, Rha SW, Seong IW, Jeong MH, Hur SH, Lee NH, Yoon J, Yang JY, Lee BK, Choi YJ, Chung WS, Lim DS, Cheong SS, Kim KS, Chae JK, Nah DY, Jeon DS, Seung KB, Jang JS, Park HS, Le Duration of Dual Antiplatelet Therapy after Implantation of Drug-Eluting Stents. N Engl J Med 2010 Mar 15;: [20231231] 10.1056/NEJMoa1001266

OPTIMIZED, :

DAPT, :

Mauri L, Kereiakes DJ, Yeh RW, Driscoll-Shempp P, Cutlip DE, Steg PG, Normand SL, Braunwald E, Wiviott SD, Cohen DJ, Holmes DR Jr, Krucoff MW, Hermiller J, Dauerman HL, Simon DI, Kandzari DE, Garratt KN, Lee DP, Pow TK, Lee PV, Rinaldi MJ, Massaro JM Twelve or 30 Months of Dual Antiplatelet Therapy after Drug-Eluting Stents. N Engl J Med 2014 Nov 16;: [25399658] 10.1056/NEJMoa1409312

6 triple antiplatelet

Trial	Treatments	Patients	Trials design and methods
triple antiplatelet vs dual antiplatelet therapy			
CILON-T , 2010 n=457/458 follow-up: 6 mo	triple antiplatelet therapy with aspirin, clopidogrel, and cilostazol for 6 month versus dual antiplatelet therapy	real-world patients undergoing PCI	Parallel groups

References

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Lee SP, Suh JW, Park KW, Lee HY, Kang HJ, Koo BK, Chae IH, Choi DJ, Rha SW, Bae JW, Cho MC, Kwon TG, Bae JH, Kim HS Study design and rationale of 'Influence of Cilostazol-based triple anti-platelet therapy on ischemic complication after drug-eluting stent implantation (CILON-T)' study: A multicenter randomized trial evaluating the efficacy of Cilostazol on ischemic vascular complications after drug-eluting stent implantation for coronary heart disease. Trials 2010;11:87 [20735821] 10.1186/1745-6215-11-87

Suh JW, Lee SP, Park KW, Lee HY, Kang HJ, Koo BK, Cho YS, Youn TJ, Chae IH, Choi DJ, Rha SW, Bae JH, Kwon TG, Bae JW, Cho MC, Kim HS Multicenter randomized trial evaluating the efficacy of cilostazol on ischemic vascular complications after drug-eluting stent implantation for coronary heart disease: results of the CILON-T (influence of CILostazol-based triple antiplatelet therapy ON ischemic complication after drug-eluting stenT implantation) trial. J Am Coll Cardiol 2011;57:280-9 [21232664] 10.1016/j.jacc.2010.08.631

7 About TrialResults-center.org

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