Clinical trials of PCSK9 Inhibitors for cardiovascular prevention in all type of patients

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1 PCSK9 Inhibitor

Trial	Treatments	Patients	Trials design and methods
alirocumab vs			
CHOICE I *ongoing* [NCT01926782] n=NA	-	-	
CHOICE II *ongoing* [NCT02023879] n=NA	-	-	
NCT01288469 *ongoing* [NCT01288469] n=NA	-	-	
evolocumab vs			
Mendel 1 , 2012 [NCT01375777] n=NA follow-up:	-	-	
MENDEl 2 [NCT01763827] n=NA	-	-	
YUKAWA-1 , 2014 n=NA follow-up:	-	-	
alirocumab vs ezetimibe (on top statin)			
ODYSSEY OPTIONS I n=NA follow-up: 24 wk	Alirocumab 75 mg with potential up-titration to 150 mg Q2W versus Ezetimibe 10 mg	high-cardiovascular-risk patients with hypercholesterolemia not adequately controlled with atorvastatin (20 or 40 mg) or rosuvastatin (10 or 20 mg)	
ODYSSEY OPTIONS II n=NA follow-up: 24 wk	Alirocumab 75 mg with potential up-titration to 150 mg Q2W versus Ezetimibe 10 mg	high-cardiovascular-risk patients with hypercholesterolemia not adequately controlled with atorvastatin (20 or 40 mg) or rosuvastatin (10 or 20 mg)	
alirocumab vs ezetimibe alone			
ODYSSEY MONO [NCT01644474] n=NA follow-up: 24 wk	Alirocumab 75 mg Q2W versus Ezetimibe 10 mg	hypercholesterolemic patients at moderate cardiovascular risk not receiving statins or other lipid-lowering therapy	double-blind

continued...

Trial	Treatments	Patients	Trials design and methods
evolocumab vs ezetimibe alone			
GAUSS 2 [NCT01763905] n=102/205 follow-up:	evolocumab 140 mg every two weeks (Q2W) or evolocumab 420 mg once monthly (QM) versus ezetimibe 10 mg	patients with statin intolerance	
bococizumab vs placebo			
SPIRE-1 *ongoing* [NCT01975376] n=NA follow-up:	Bococizumab versus placebo	high risk subjects who are receiving background lipid lowering therapy and have cholesterol laboratory values of LDL-C >/= 70 mg/dL (1.8 mmol/L) and <100 mg/dL (2.6 mmol/L) or non-HDL-C >/= 100 mg /dl (2.6 mmol/L) and <130 mg/dL (3.4 mmol/L).	double-blind
SPIRE-2 *ongoing* [NCT01975389] n=NA follow-up:	bococizumab versus Placebo	high risk subjects who are receiving background lipid lowering therapy and have cholesterol laboratory values of LDL-C >/= 100 mg/dL (2.6 mmol/L) or non-HDL-C >/=130 mg/dL (3.4 mmol/L).	double-blind
SPIRE-FH *ongoing* [NCT01968980] n=NA follow-up:	-	subjects with heterozygous familial hypercholesterolemia receiving highly effective statins	double-blind US
SPIRE-HR *ongoing* [NCT01968954] n=NA follow-up:	Bococizumab versus Placebo	subjects with high cholesterol receiving highly effective statins	double-blind US
SPIRE-LDL *ongoing* [NCT01968967] n=NA follow-up:	-	subjects with high cholesterol receiving highly effective statins	double-blind US
SPIRE-LL *ongoing* [NCT02100514] n=NA follow-up:	-	subjects with hyperlipidemia receiving background statin therapy	double-blind US
SPIRE-SI *ongoing* [NCT02135029] n=NA follow-up:	Bococizumab versus Placebo	-	double-blind
evolocumab vs placebo			
GAUSS 1 , 2012 [NCT01375764] n=95/32 follow-up:	-	statin-intolerant patients	
alirocumab vs placebo (on top statins)			

continued...

Trial	Treatments	Patients	Trials design and methods
ODYSSEY Alternative [NCT01709513] n=NA follow-up: 65279;24 wk	Alirocumab 75 mg with potential up-titration to 150 mg Q2W versus Ezetimibe 10 mg	statin-intolerant patients	double-blind
ODYSSEY COMBO [NCT01644175] n=NA follow-up: 52 wk	Alirocumab 75 mg with potential up-titration to 150 mg Q2W versus Placebo	high cardiovascular risk patients on maximally tolerated statin therapy	double-blind
ODYSSEY COMBO II [NCT01644188] n=NA follow-up: 104 wk	Alirocumab 75 mg with potential up-titration to 150 mg Q2W versus Ezetimibe 10 mg	high cardiovascular risk patients with inadequately controlled hypercholesterolaemia on maximally tolerated doses of statins	double-blind
ODYSSEY FH 1 [NCT01623115] n=NA follow-up: 78 wk	Alirocumab 75 mg with potential up-titration to 150 mg Q2W versus Placebo	patients with heterozygous familial hypercholesterolemia not adequately controlled with current lipid-lowering therapy	double-blind
ODYSSEY FH 2 [NCT01709500] n=NA follow-up: 78 wk	Alirocumab 75 mg with potential up-titration to 150 mg Q2W versus Placebo	patients with heterozygous familial hypercholesterolemia not adequately controlled with current lipid-lowering therapy	double blind
ODYSSEY HIGH FH [NCT01617655] n=NA follow-up: 5278 wk	Alirocumab 150 mg Q2W versus Placebo	patients with heterozygous familial hypercholesterolemia not adequately controlled with current lipid-lowering therapy	
ODYSSEY Long-Term , 2015 [NCT01507831] n=1553/788 follow-up: 78 wk	alirocumab 150 mg as a 1-ml subcutaneous injection every 2 weeks for 78 weeks. versus placebo	patients at high risk for cardiovascular events who had LDL cholesterol levels of 70 mg per deciliter (1.8 mmol per liter) or more and were receiving treatment with statins at the maximum tolerated dose (the highest dose associated with an acceptable side-effect profile), with or without other lipid-lowering therapy	
ODYSSEY OUTCOMES , 2018 [NCT01663402] n=9462/9462 follow-up: 2.8 yr (median)	Alirocumab (on top intensive or maximum-tolerated statin therapy) versus placebo	Post-ACS patients (1 to 12 months)with elevated levels of atherogenic lipoproteins despite intensive or maximum-tolerated statin therapy	Parallel groups double-blind 57 countries
evolocumab vs placebo (on top statins)			
DESCARTES , 2014 [NCT01516879] n=599/302 follow-up: 52 weeks	evolocumab (420 mg) every 4 weeks versus placebo	-	
FOURIER , 2017 [NCT01764633] n=NA follow-up: 2.2 years	evolocumab (either 140 mg every 2 weeks or 420 mg monthly) versus placebo	patients with atherosclerotic cardiovascular disease and LDL cholesterol levels of 70 mg per deciliter (1.8 mmol per liter) or higher who were receiving statin therapy	Parallel groups double-blind

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Trial	Treatments	Patients	Trials design and methods
LAPLACE 2 , 2014 [NCT01763866] n=1117/558 follow-up:	evolucumab + statin versus placebo + statin	-	
LAPLACE-TIMI 57 [NCT01380730] n=NA follow-up:	subcutaneous injections of AMG 145 70 mg, 105 mg, or 140 mg, versus placebo	-	
RUTHERFORD-1 [NCT01375751] n=111/56 follow-up:	AMG 145 350 mg, AMG 145 420 mg versus placebo	heterozygous familial hypercholesterolemia patients	
RUTHERFORD-2 , 2015 [NCT01763918] n=220/109 follow-up:	subcutaneous evolocumab 140 mg every 2 weeks, evolocumab 420 mg monthly versus placebo	heterozygous familial hypercholesterolaemia	

References

CHOICE I , :

CHOICE II , :

NCT01288469, :

Mendel 1, 2012:

Koren MJ, Scott R, Kim JB, Knusel B, Liu T, Lei L, Bolognese M, Wasserman SM Efficacy, safety, and tolerability of a monoclonal antibody to proprotein convertase subtilisin/kexin type 9 as monotherapy in patients with hypercholesterolaemia (MENDEL): a randomised, double-blind, placebo-controlled, phase 2 study. Lancet 2012 Dec 8;380:1995-2006 [23141812] 10.1016/S0140-6736(12)61771-1

MENDEl 2, :

YUKAWA-1, 2014:

Hirayama A, Honarpour N, Yoshida M, Yamashita S, Huang F, Wasserman SM, Teramoto T Effects of evolocumab (AMG 145), a monoclonal antibody to PCSK9, in hypercholesterolemic, statin-treated Japanese patients at high cardiovascular risk–primary results from the phase 2 YUKAWA study. Circ J 2014;78:1073-82 [24662398]

ODYSSEY OPTIONS I, :

Robinson JG, Colhoun HM, Bays HE, Jones PH, Du Y, Hanotin C, Donahue S Efficacy and safety of alirocumab as add-on therapy in high-cardiovascular-risk patients with hypercholesterolemia not adequately controlled with atorvastatin (20 or 40 mg) or rosuvastatin (10 or 20 mg): design and rationale of the ODYSSEY OPTIONS Studies. Clin Cardiol 2014 Oct;37:597-604 [25269777]

Bays H, Gaudet D, Weiss R, Ruiz JL, Watts GF, Gouni-Berthold I, Robinson J, Zhao J, Hanotin C, Donahue S Alirocumab as Add-on To Atorvastatin Versus Other Lipid Treatment Strategies: ODYSSEY OPTIONS I Randomized Trial. J Clin Endocrinol Metab 2015 Jun 1;:jc20151520 [26030325]

ODYSSEY OPTIONS II, :

Robinson JG, Colhoun HM, Bays HE, Jones PH, Du Y, Hanotin C, Donahue S Efficacy and safety of alirocumab as add-on therapy in high-cardiovascular-risk patients with hypercholesterolemia not adequately controlled with atorvastatin (20 or 40 mg) or rosuvastatin (10 or 20 mg): design and rationale of the ODYSSEY OPTIONS Studies. Clin Cardiol 2014 Oct;37:597-604 [25269777]

ODYSSEY MONO, :

Roth EM, Taskinen MR, Ginsberg HN, Kastelein JJ, Colhoun HM, Robinson JG, Merlet L, Pordy R, Baccara-Dinet MT Monotherapy with the PCSK9 inhibitor alirocumab versus ezetimibe in patients with hypercholesterolemia: results of a 24 week, double-blind, randomized Phase 3 trial. Int J Cardiol 2014;176:55-61 [25037695]

GAUSS 2, :

Stroes E, Colquhoun D, Sullivan D, Civeira F, Rosenson RS, Watts GF, Bruckert E, Cho L, Dent R, Knusel B, Xue A, Scott R, Wasserman SM, Rocco M Anti-PCSK9 antibody effectively lowers cholesterol in patients with statin intolerance: the GAUSS-2 randomized, placebo-controlled phase 3 clinical trial of evolocumab. J Am Coll Cardiol 2014 Jun 17;63:2541-8 [24694531]

SPIRE-1, 0:

SPIRE-2, 0:

SPIRE-FH, 0:

SPIRE-HR, 0:

SPIRE-LDL, 0:

SPIRE-LL, 0:

SPIRE-SI, 0:

GAUSS 1, 2012:

Sullivan D, Olsson AG, Scott R, Kim JB, Xue A, Gebski V, Wasserman SM, Stein EA Effect of a monoclonal antibody to PCSK9 on low-density lipoprotein cholesterol levels in statin-intolerant patients: the GAUSS randomized trial. JAMA 2012 Dec 19;308:2497-506 [23128163]

ODYSSEY Alternative, :

Moriarty PM, Jacobson TA, Bruckert E, Thompson PD, Guyton JR, Baccara-Dinet MT, Gipe D Efficacy and safety of alirocumab, a monoclonal antibody to PCSK9, in statin-intolerant patients: design and rationale of ODYSSEY ALTERNATIVE, a randomized phase 3 trial. J Clin Lipidol 2014;8:554-61 [25499937]

ODYSSEY COMBO, :

Kereiakes DJ, Robinson JG, Cannon CP, Lorenzato C, Pordy R, Chaudhari U, Colhoun HM Efficacy and safety of the proprotein convertase subtilisin/kexin type 9 inhibitor alirocumab among high cardiovascular risk patients on maximally tolerated statin therapy: The ODYSSEY COMBO I study. Am Heart J 2015;169:906-915.e13 [26027630]

Colhoun HM, Robinson JG, Farnier M, Cariou B, Blom D, Kereiakes DJ, Lorenzato C, Pordy R, Chaudhari U Efficacy and safety of alirocumab, a fully human PCSK9 monoclonal antibody, in high cardiovascular risk patients with poorly controlled hypercholesterolemia on maximally tolerated doses of statins: rationale and design of the ODYSSEY COMBO I and II trials. BMC Cardiovasc Disord 2014;14:121 [25240705]

ODYSSEY COMBO II, :

Colhoun HM, Robinson JG, Farnier M, Cariou B, Blom D, Kereiakes DJ, Lorenzato C, Pordy R, Chaudhari U Efficacy and safety of alirocumab, a fully human PCSK9 monoclonal antibody, in high cardiovascular risk patients with poorly controlled hypercholesterolemia on maximally tolerated doses of statins: rationale and design of the ODYSSEY COMBO I and II trials. BMC Cardiovasc Disord 2014;14:121 [25240705]

Cannon CP, Cariou B, Blom D, McKenney JM, Lorenzato C, Pordy R, Chaudhari U, Colhoun HM Efficacy and safety of alirocumab in high cardiovascular risk patients with inadequately controlled hypercholesterolaemia on maximally tolerated doses of statins: the ODYSSEY COMBO II randomized controlled trial. Eur Heart J 2015;36:1186-94 [25687353]

ODYSSEY FH 1, :

Kastelein JJ, Robinson JG, Farnier M, Krempf M, Langslet G, Lorenzato C, Gipe DA, Baccara-Dinet MT Efficacy and safety of alirocumab in patients with heterozygous familial hypercholesterolemia not adequately controlled with current lipid-lowering therapy: design and rationale of the ODYSSEY FH studies. Cardiovasc Drugs Ther 2014;28:281-9 [24842558]

ODYSSEY FH 2, :

Kastelein JJ, Robinson JG, Farnier M, Krempf M, Langslet G, Lorenzato C, Gipe DA, Baccara-Dinet MT Efficacy and safety of alirocumab in patients with heterozygous familial hypercholesterolemia not adequately controlled with current lipid-lowering therapy: design and rationale of the ODYSSEY FH studies. Cardiovasc Drugs Ther 2014;28:281-9 [24842558]

ODYSSEY HIGH FH , :

Kastelein JJ, Robinson JG, Farnier M, Krempf M, Langslet G, Lorenzato C, Gipe DA, Baccara-Dinet MT Efficacy and safety of alirocumab in patients with heterozygous familial hypercholesterolemia not adequately controlled with current lipid-lowering therapy: design and rationale of the ODYSSEY FH studies. Cardiovasc Drugs Ther 2014;28:281-9 [24842558]

ODYSSEY Long-Term, 2015:

Robinson JG, Farnier M, Krempf M, Bergeron J, Luc G, Averna M, Stroes ES, Langslet G, Raal FJ, Shahawy ME, Koren MJ, Lepor NE, Lorenzato C, Pordy R, Chaudhari U, Kastelein JJ Efficacy and Safety of Alirocumab in Reducing Lipids and Cardiovascular Events. N Engl J Med 2015 Mar 15;: [25773378] 10.1056/NEJMoa1501031

ODYSSEY OUTCOMES, 2018:

Schwartz GG, Bessac L, Berdan LG, Bhatt DL, Bittner V, Diaz R, Goodman SG, Hanotin C, Harrington RA, Jukema JW, Mahaffey KW, Moryusef A, Pordy R, Roe MT, Rorick T, Sasiela WJ, Shirodaria C, Szarek M, Tamby JF, Tricoci P, White H, Zeiher A, Steg PG Effect of alirocumab, a monoclonal antibody to PCSK9, on long-term cardiovascular outcomes following acute coronary syndromes: rationale and design of the ODYSSEY outcomes trial. Am Heart J 2014;168:682-9 [25440796]

DESCARTES, 2014:

Blom DJ, Hala T, Bolognese M, Lillestol MJ, Toth PD, Burgess L, Ceska R, Roth E, Koren MJ, Ballantyne CM, Monsalvo ML, Tsirtsonis K, Kim JB, Scott R, Wasserman SM, Stein EA A 52-week placebo-controlled trial of evolocumab in hyperlipidemia. N Engl J Med 2014 May 8;370:1809-19 [24678979]

FOURIER, 2017:

Sabatine MS, Giugliano RP, Keech AC, Honarpour N, Wiviott SD, Murphy SA, Kuder JF, Wang H, Liu T, Wasserman SM, Sever PS, Pedersen TR Evolocumab and Clinical Outcomes in Patients with Cardiovascular Disease. N Engl J Med 2017;376:1713-1722 [28304224]

LAPLACE 2, 2014:

Robinson JG, Nedergaard BS, Rogers WJ, Fialkow J, Neutel JM, Ramstad D, Somaratne R, Legg JC, Nelson P, Scott R, Wasserman SM, Weiss R Effect of evolocumab or ezetimibe added to moderate- or high-intensity statin therapy on LDL-C lowering in patients with hypercholesterolemia: the LAPLACE-2 randomized clinical trial. JAMA 2014 May 14;311:1870-82 [24825642]

LAPLACE-TIMI 57, :

Giugliano RP, Desai NR, Kohli P, Rogers WJ, Somaratne R, Huang F, Liu T, Mohanavelu S, Hoffman EB, McDonald ST, Abrahamsen TE, Wasserman SM, Scott R, Sabatine MS Efficacy, safety, and tolerability of a monoclonal antibody to proprotein convertase subtilisin/kexin type 9 in combination with a statin in patients with hypercholesterolaemia (LAPLACE-TIMI 57): a randomised, placebo-controlled, dose-ranging, phase 2 study. Lancet 2012 Dec 8;380:2007-17 [23141813]

RUTHERFORD-1, :

Raal F, Scott R, Somaratne R, Bridges I, Li G, Wasserman SM, Stein EA Low-density lipoprotein cholesterol-lowering effects of AMG 145, a monoclonal antibody to proprotein convertase subtilisin/kexin type 9 serine protease in patients with heterozygous familial hypercholesterolemia: the Reduction of LDL-C with PCSK9 Inhibition in Heterozygous Familial Hypercholesterolemia Disorder (RUTHERFORD) randomized trial. Circulation 2012 Nov 13;126:2408-17 [23129602]

RUTHERFORD-2, 2015:

Raal FJ, Stein EA, Dufour R, Turner T, Civeira F, Burgess L, Langslet G, Scott R, Olsson AG, Sullivan D, Hovingh GK, Cariou B, Gouni-Berthold I, Somaratne R, Bridges I, Scott R, Wasserman SM, Gaudet D PCSK9 inhibition with evolocumab (AMG 145) in heterozygous familial hypercholesterolaemia (RUTHERFORD-2): a randomised, double-blind, placebo-controlled trial. Lancet 2015 Jan 24;385:331-40 [25282519]

2 About TrialResults-center.org

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