EVALUATION OF CARDIOVASCULAR EVENTS ON KOREAN DYSLIPIDEMIC PATIENTS WITH FENOFIBRATE TREATMENT IN THE REAL WORLD

ECLIPSE-REAL

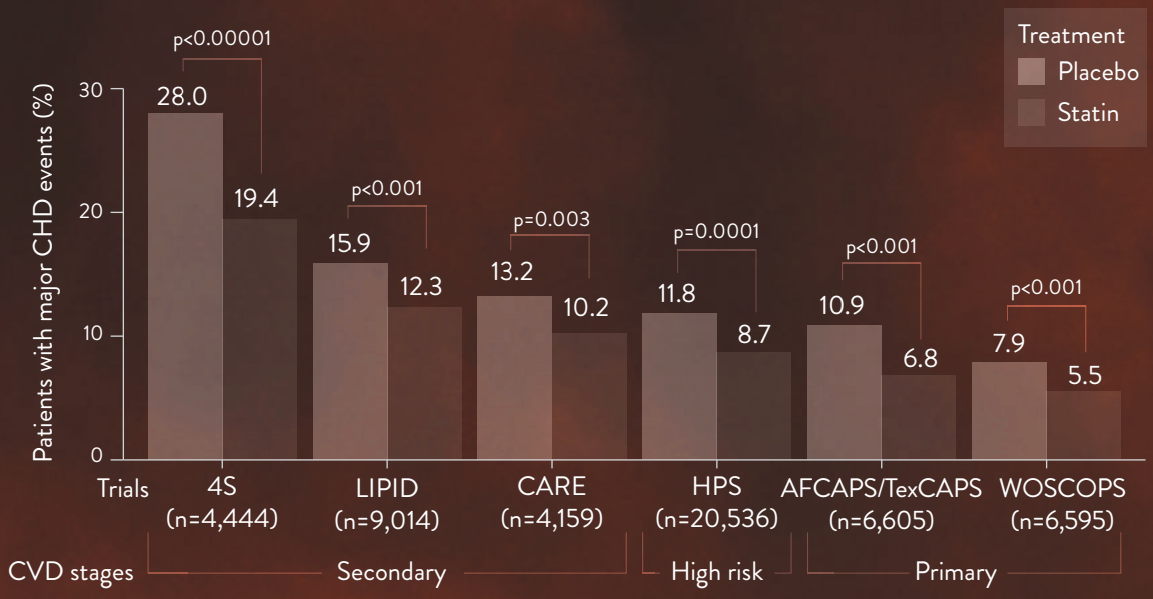
LIPANTHYL® PENTA 145

145 mg Fenofibrate

HKG2148848

Over 6 in 10 statin users remain at a high residual CVD risk[1-6]

Residual CVD risk in statin vs. placebo trials[1-6]



Dyslipidemia is a common CVD risk-enhancing factor in Asia[7-9]

Prevalence (%) of dyslipidemia in the U.S. and Asia[9]

	The U.S. population	Asian population
Year	1999–2006	2007
n	6,962	2,890
TG*	32.0	33.2
Men	36.1	40.8
Women	27.6	27.8
HDL-C	30.7	50.2
Men†	27.6	34.7
Women†	33.8	59.3

Statin may be insufficient for the prevention of CVD.
In Asia, one of the common risk factors of CVD is dyslipidemia[1-9]

* Individual with TG ≥1.69 mmol/L or medication use was considered as hypertriglyceridemia.[9] † HDL-C <1.03 mmol/L in men, <1.29 mmol/L in women, or those with medication use was considered as low HDL-C.[9]

4S=the Scandinavian Simvastatin Survival Study; AHA=American Heart Association; AFCAPS/TexCAPS=The Air Force/Texas Coronary Atherosclerosis Prevention Study; CARE=The Cholesterol and Recurrent Events; CHD=coronary heart disease; CVD=cardiovascular disease; ESC=European Society of Cardiology; HDL-C=high density lipoprotein-cholesterol; HPS=Heart Protection Study; LIPID=Long-Term Intervention with Pravastatin in Ischaemic Disease; TG=triglyceride; WOSCOPS=The West of Scotland Coronary Prevention Study.

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ECLIPSE is so REAL

The patient cohort is so FOCUSED:

Comparison of settings between ECLIPSE-REAL study and other trials for evaluating the relative CV risk in Lipanthyl®-based regimens

	ECLIPSE-REAL[10]	ACCORD-Lipid[11]	FIELD[12]
Treatment arms	Lipanthyl® and statin combination therapy vs. statin monotherapy	Lipanthyl® and simvastatin combination therapy vs. simvastatin monotherapy	Lipanthyl® vs. placebo
Study Region	Asia	North America	South Pacific Ocean and Europe
Patient condition	Metabolic syndrome	Diabetes	Diabetes
Median TG level at baseline (mmol/L)	2.35	1.83	1.73

The statistical analysis is so RELIABLE:

- ECLIPSE-REAL derived the propensity score model from a multiple logistic regression to balance the covariates between study arms[10]
- Independent variables included:

Basic characteristic	Body measurement	Plasma lipid level	CVD history and medication	Personal habit
Age	Waist circumference	Baseline LDL-C levels*	Preexsisting CVD§	Smoking status#
Sex	Fasting glucose level	Baseline HDL-C levels†	Antithrombotic agents	Alcohol consumption^
	Systolic blood pressure	Baseline TG levels‡	Antihypertensive agents	Physical activity$
	Serum creatinine level		Statin intensity and duration¶	

ECLIPSE-REAL demonstrated CV outcomes of Lipanthyl® add-on therapy among Asian patients with metabolic syndrome in the real-world setting[10]

*Baseline LDL-C levels were stratified by <2.59, 2.59–3.36, 3.36–4.14 and 4.14 mmol/L.[10] †According to previous clinical trials, HDL-C levels were stratified by <0.88, 0.88 mmol/L.[10] ‡According to previous clinical trials, TG levels were stratified by <2.3, 2.3 mmol/L.[10] §Preexisting CVD included coronary heart disease, ischaemic stroke and heart failure.[10] ¶Statin intensity was based on the average expected LDL-C response and duration represented the period of statin treatment before the index date.[10] #Smoking status included current, former or never.[10] ^Alcohol consumption included 3 times a week, twice a week, or never.[10] $Frequency of physical activity included 3 times a week, twice a week, or never.[10]

ACCORD-Lipid=The Action to Control Cardiovascular Risk in Diabetes-Lipid; CV=cardiovascular; CVD=cardiovascular disease; ECLIPSE-REAL=Evaluation of cardiovascular events on Korean dyslipidemic patients with fenofibrate treatement in the real world; FIELD=The Fenofibrate Intervention and Event Lowering in Diabetes; HDL-C=high density lipoprotein-cholesterol; LDL-C=low density lipoprotein-cholesterol; TG=triglyceride.

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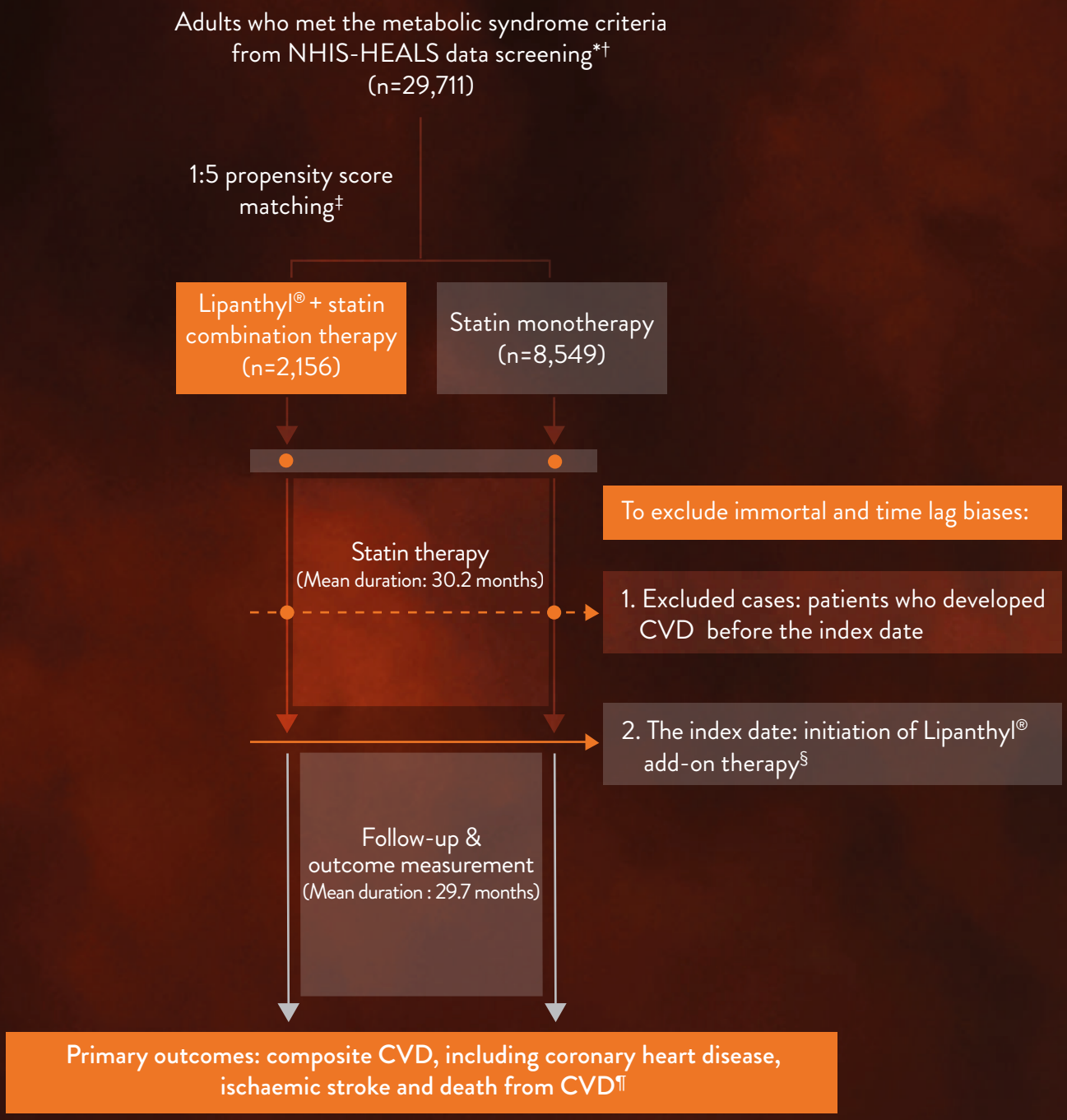
Study design of ECLIPSE-REAL[10]

A retrospective, real-world, propensity weighted cohort study



ECLIPSE-REAL evaluated the effect of Lipanthyl® add-on therapy on the reduction of residual CVD risk in patients with metabolic syndrome within a real world database[10]

* Adults aged ≥40 years from the original database had used statin for at least three months from 1 January 2007 to 31 December 2014, as the national health examination programmes included lipid profiles from January 2007. Adults without documented lipid profiles before initiation of statin treatment were excluded.[10] † Metabolic syndrome criteria was defined by the Adult Treatment Panel III guidelines, before the index date. Adults with metabolic syndrome were required to meet three or more of the following criteria: (1) waist circumference ≥90 cm in men and ≥80 cm in women, (2) serum TG ≥1.7 mmol/L, (3) HDL-C<1.0 mmol/L in men and <1.3 mmol/L in women, (4) fasting glucose ≥5.6 mmol/L or antidiabetes treatment, and (5) blood pressure ≥130/85 mmHg or treatment for hypertension.[10] ‡ Independent variables in the propensity score model were age, sex, waist circumference, fasting glucose level, systolic blood pressure, serum creatinine level, smoking status, alcohol consumption, physical activity, preexsisting CV disease, antithrombotic agents, antihypertensive agents, statin intensity based on the average expected LDL-C response, duration of statin treatment before the index date. Baseline levels of LDL-C, HDL-C and TG were also included.[10] § The index date was defined as 3 months after initiating statin treatment.[10] ¶ The composite CVD outcomes were defined as followed: incident coronary heart disease=ICD-10 codes I20-I25 plus a coronary artery angiography procedure, ischaemic stroke=ICD-10 codes I63-66 with an examination of brain imaging studies or procedures, and death from cardiovascular disease=ICD codes I00-I99.[10]

CVD=cardiovascular disease; ECLIPSE-REAL=Evaluation of cardiovascular events on Korean dyslipidemic patients with fenofibrate treatement in the real world; HDL-C=high density lipoprotein-cholesterol; NHIS-HEALS=Korean National Health Insurance Service-Health Screening Cohort; LDL-C=low density lipoprotein-cholesterol; SD=standard deviation; TG=triglyceride.

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Participants baseline characteristics in ECLIPSE-REAL

General properties of adults (%, n) in the study[10]

Type 2 diabetes | Hypertriglyceridemia* | Metabolic syndrome | Preexsisting CVD events | Low HDL-C*

Baseline characteristics (%, numbers) of adults in treatment arms†[10]

Characteristics	Combination therapy of Lipanthyl® and statin (n=2,156)	Statin monotherapy (n=8,549)	Absolute standardized difference	
			Before PS matching	After PS matching
Age (mean±SD, years)	62.3±7.9	62.6±8.0	0.39	0.03
Men	54.2 (1,169)	52.7 (4,505)	0.26	0.03
Comorbidities				
Coronary heart disease	3.5 (75)	4.2 (360)	0.15	0.04
Ischemic stroke	3.9 (85)	4.4 (377)	0.08	0.02
Heart failure	1.4 (31)	1.4 (122)	0.07	<0.01
Statin intensity‡			**0.06**	**0.03**
High	2.4 (51)	2.3 (193)	-	-
Moderate	92.4 (1,991)	93.0 (7,949)	-	-
Low	5.3 (114)	4.8 (407)	-	-
HDL-C (mmol/L)			**0.13**	**0.01**
<0.88	8.6 (186)	8.2 (705)	-	-
≥0.88	91.4 (1,970)	91.8 (7,844)	-	-
TG (mmol/L)			**0.71**	**0.11§**
<2.3	43.5 (937)	48.7 (4,164)	-	-
≥2.3	56.5 (1,219)	51.3 (4,385)	-	-

- Mean LDL-C and HDL-C levels were well balanced between the groups[10]
- The mean of TG in the combination therapy group with Lipanthyl® was higher than the monotherapy group[10]

*HDL-C and TG were matched by prespecified cut-offs (0.88 mmol/L and and 2.3 mmol/L, respectively) for lower and higher levels of each variable. [10] †Unless stated otherwise.[10] ‡Defined based on average expected LDL-C response.[10] §Absolute standardized dierence0.1 after PS matching.[10]

CVD=cardiovascular disease; ECLPSE-REAL=Evaluation of cardiovascular events on Korean dyslipidemic patients with fenofibrate treatement in the real world; HDL-C=high density lipoprotein-cholesterol; LDL-C=low density lipoprotein-cholesterol; PS=propensity score; TG=triglyceride.

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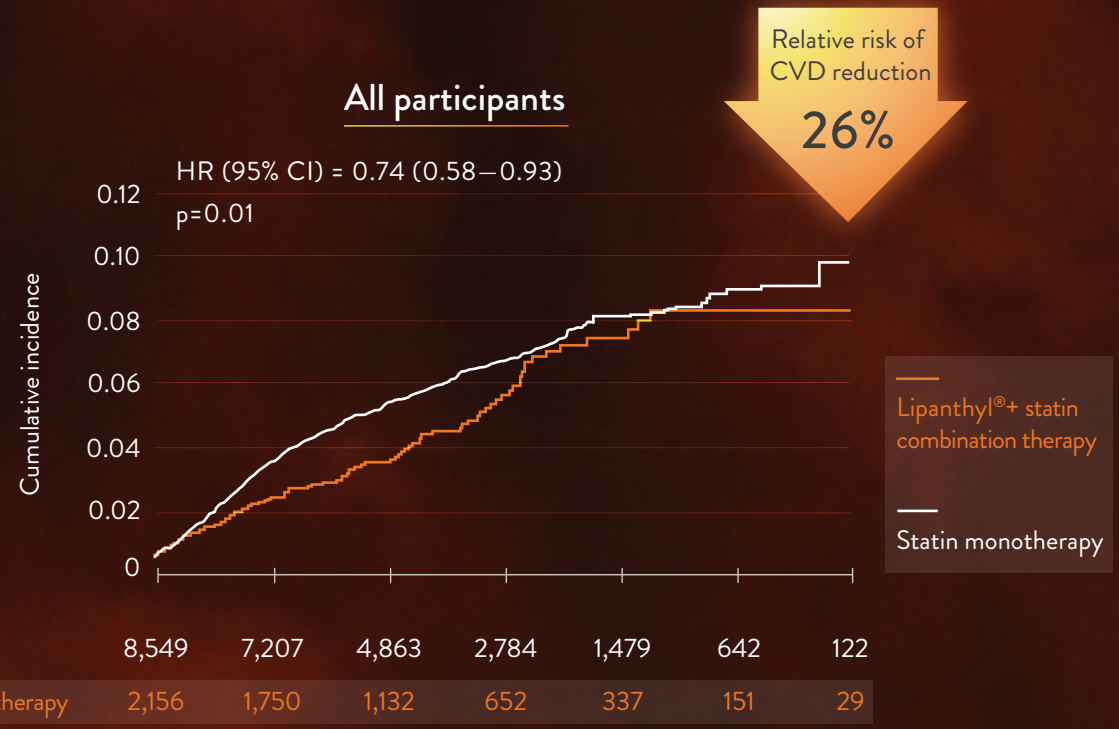
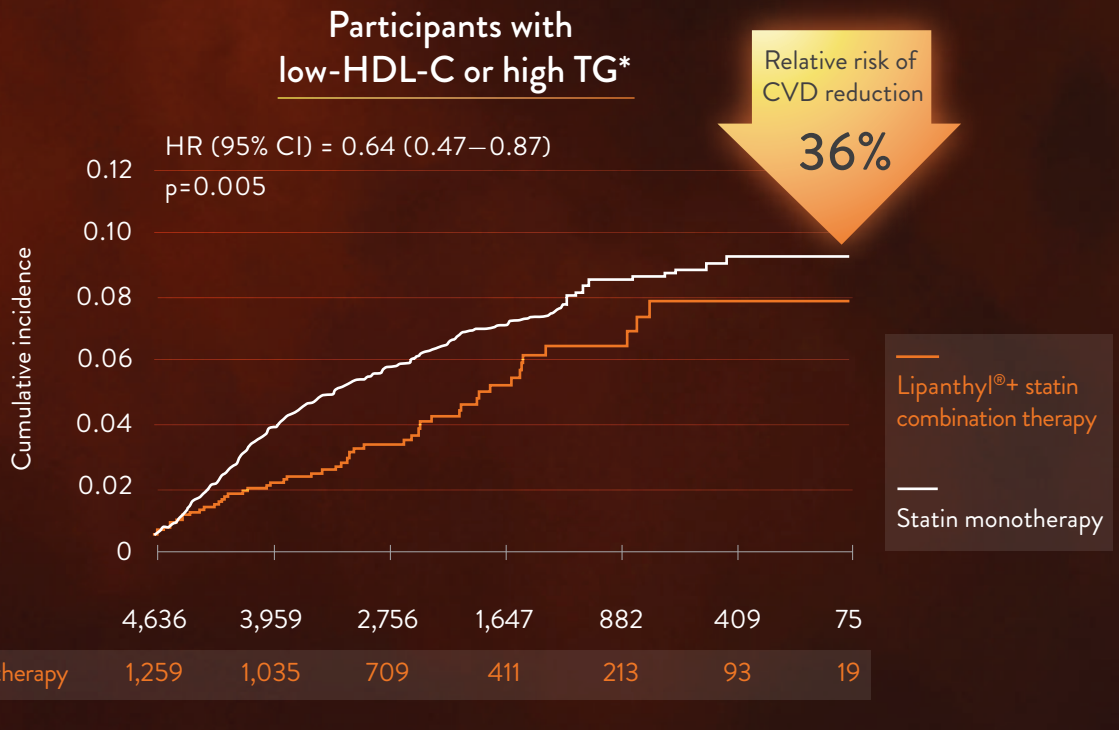
Lipanthyl® significantly reduced the risk of composite CVD on top of statin therapy[10]

All participants



No at risk							
Statin monotherapy	8,549	7,207	4,863	2,784	1,479	642	122
Lipanthyl®+ statin combination therapy	2,156	1,750	1,132	652	337	151	29

Participants with low-HDL-C or high TG*



No at risk							
Statin monotherapy	4,636	3,959	2,756	1,647	882	409	75
Lipanthyl®+ statin combination therapy	1,259	1,035	709	411	213	93	19

Combination therapy of Lipanthyl® and statin significantly reduced the relative risk of major CVD by 26% and 36% in overall and dyslipidemia cohorts respectively[10]

* Low HDL-C was defined by the level of HDL-C ≤0.88 mmol/L. High TG represented by the level of TG ≥2.3 mmol/L.[10]

CI=confidence interval; CVD=cardiovascular disease; HDL-C=high density lipoprotein-cholesterol; HR=hazard ratio; TG=triglyceride.

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Lipanthyl® was related to a lower risk of composite CVD across subgroups, compared with statin monotherapy[10]

Subgroup	Lipanthyl® + statin combination therapy	Statin monotherapy	p-value
Age (years)	No of events/total		0.8
≥65	46/818	255/3,302	
<65	44/1,338	216/5,247	
Sex			0.8
Men	58/1,169	295/4,505	
Women	32/987	176/4,044	
Waist circumference (cm)			0.7
≥90	36/839	197/3,305	
<90	54/1,317	274/5,244	
Underlying CVD			0.7
Yes	27/177	149/803	
No	63/1,979	322/7,746	
Hypertension			0.5
Yes	76/1,691	402/6,608	
No	14/465	69/1,941	
Type 2 diabetes			0.9
Yes	47/879	226/3,165	
No	43/1,277	245/5,384	
LDL-C (mmol/L)			0.09
<2.59	34/877	175/3,356	
2.59–3.36	16/549	122/2,125	
≥3.36	40/730	174/3,068	
HDL-C (mmol/L)			0.6
≥0.88	81/1,970	418/7,844	
<0.88	9/186	53/705	
TG (mmol/L)			0.2
≥2.30	47/1,219	260/4,385	
<2.30	43/937	211/4,164	
Non-HDL-C (mmol/L)			0.8
≥3.36	71/1,616	343/6,019	
<3.36	19/540	127/2,528	
HDL-C/TG			0.2
Low HDL-C or high TG	50/1,259	281/4,636	
High HDL-C and low TG	40/897	190/3,913	
On treatment LDL-C (mmol/L)			0.2
≥2.59	14/329	57/1,469	
<2.59	14/409	114/2,185	

ECLIPSE-REAL study proved the combination therapy of Lipanthyl® and statin decreased the relative risk of major CVD across subgroups[10]

CI=confidence interval; CVD=cardiovascular disease;
ECLIPSE-REA=Evaluation of cardiovascular events on Korean dyslipidemic patients with fenofibrate treatement in the real world;
HDL-C=high density lipoprotein-cholesterol; HR=hazard ratio; LDL-C=low density lipoprotein-cholesterol; TG=triglyceride.

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ECLIPSE-REAL study demonstrated that:

Lipanthyl® add-on therapy

- significantly reduced the risk of major CVD outcomes by 26% in participants with metabolic syndrome and 36% in dyslipidemia, compared with statin monotherapy[10]
- reduced the relative risk of CVD across subgroups[10]
- AHA and ESC/EAS guidelines recommend Lipanthyl® add-on therapy for statin-treated patients with persistently high level of TG[7,8]

AHA=American Heart Association; CVD=cardiovascular diseases; EAS=European Atherosclerosis Society;
ECLIPSE-REAL=Evaluation of cardiovascular events on Korean dyslipidemic patients with fenofibrate treatement in the real world; ESC=European Society of Cardiology; TG=triglyceride.

ECLIPSE-REAL

References: 1. Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S). Lancet 1994; 344(8934): 1383-9. **2.** Prevention of cardiovascular events and death with pravastatin in patients with coronary heart disease and a broad range of initial cholesterol levels. N Engl J Med 1998; 339(19): 1349-57. **3.** MRC/BHF Heart Protection Study of antioxidant vitamin supplementation in 20,536 high-risk individuals: a randomised placebo-controlled trial. Lancet 2002; 360(9326): 23-33. **4.** Downs JR, Clearfield M, Weis S, et al. Primary prevention of acute coronary events with lovastatin in men and women with average cholesterol levels: results of AFCAPS/TexCAPS. Air Force/Texas Coronary Atherosclerosis Prevention Study. Jama 1998; 279(20): 1615-22. **5.** Sacks FM, Pfeffer MA, Moye LA, et al. The effect of pravastatin on coronary events after myocardial infarction in patients with average cholesterol levels. Cholesterol and Recurrent Events Trial investigators. N Engl J Med 1996; 335(14): 1001-9. **6.** Shepherd J, Cobbe SM, Ford I, et al. Prevention of coronary heart disease with pravastatin in men with hypercholesterolemia. West of Scotland Coronary Prevention Study Group. N Engl J Med 1995; 333(20): 1301-7. **7.** Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation 2019; 139(25): e1082-e143. **8.** Mach F, Baigent C, Catapano AL, et al. 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. Eur Heart J 2020; 41(1): 111-88. **9.** Lim S, Shin H, Song JH, et al. Increasing prevalence of metabolic syndrome in Korea: the Korean National Health and Nutrition Examination Survey for 1998-2007. Diabetes Care 2011; 34(6): 1323-8. **10.** Kim NH, Han KH, Choi J, Lee J, Kim SG. Use of fenofibrate on cardiovascular outcomes in statin users with metabolic syndrome: propensity matched cohort study. Bmj 2019; 366: l5125. **11.** Ginsberg HN, Elam MB, Lovato LC, et al. Effects of combination lipid therapy in type 2 diabetes mellitus. N Engl J Med 2010; 362(17): 1563-74. **12.** Keech A, Simes RJ, Barter P, et al. Effects of long-term fenofibrate therapy on cardiovascular events in 9795 people with type 2 diabetes mellitus (the FIELD study): randomised controlled trial. Lancet 2005; 366(9500): 1849-61.

Lipanthyl Penta 145mg abbreviated prescribing information.
Lipanthyl Penta 145mg PI: One film-coated tablet contains 145.0 mg fenofibrate (nanoparticles). **Indications:** as an adjunct to diet and other non-pharmacological treatment for the following conditions: severe hypertriglyceridemia w/ or w/o low HDL cholesterol; mixed hyperlipidemia when statin is contraindicated or not tolerated; mixed hyperlipidemia in pts at high CV risk in addition to a statin when triglycerides and HDL cholesterol are not adequately controlled. **Recommended dosage:** 1 film-coated tablet (containing 145mg fenofibrate) once daily. Tablets should be swallowed whole with or without **Contraindications:** Hypersensitivity. Hepatic & renal insufficiency. Photoallergy orphototoxic reaction. Gallbladder disease. Chronic or acute pancreatitis (w/ exception due to severe hypertriglyceridemia). Allergy to peanut, arachis oil, soya lecithin or related products. Fructose intolerance. Lactase deficiency. Glucose-galactose malabsorption. **Special Precautions:** Secondary cause of hypercholesterolemia; concurrent estrogen or estrogen-containing contraceptives; monitor transaminase levels 3 mthly in the 1st yr of therapy; pancreatitis; myotoxicity; rhabdomyolysis; increased creatinine levels. **Common ADR:** Digestive, gastric or intestinal disorder (abdominal pain, nausea, vomiting, diarrhoea, flatulence). Elevated levels of serum transaminases.

For healthcare professional only. Full prescribing information available on request.

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