

Rosuvastatin- Ezetimibe

Tehran.Dec 2022

ACTOVERCO

Together for a healthy future

Ezetimibe

- **Brand Names:**

US Zetia

- **Pharmacologic Category:**

Antilipemic Agent, 2-Azetidinone

- **Mechanism of Action:**

Inhibits absorption of cholesterol at the brush border of the small intestine via the sterol transporter, Niemann-Pick C1-Like1 (NPC1L1). This leads to a decreased delivery of cholesterol to the liver, reduction of hepatic cholesterol stores, and increased clearance of cholesterol from the blood; it decreases total C, LDL-cholesterol (LDL-C), ApoB, and triglycerides (TG) while increasing HDL-cholesterol (HDL-C).



2019 ESC/EAS Guidelines for the management of dyslipidaemias: *lipid modification to reduce cardiovascular risk*



Recommendations for pharmacological low-density lipoprotein cholesterol lowering (1)

Recommendations	Class	Level
It is recommended to prescribe a high-intensity statin up to the highest tolerated dose to reach the goals ^c set for the specific level of risk.	I	A
If the goals ^c are not achieved with the maximum tolerated dose of statin, combination with ezetimibe is recommended.	I	B
For primary prevention patients at very-high risk, but without FH, if the LDL-C goal is not achieved on a maximum tolerated dose of statin and ezetimibe, a combination with a PCSK9 inhibitor may be considered.	IIb	C

© ESC

^c For definitions see Full Text

www.escardio.org/guidelines

2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk (European Heart Journal 2019 -doi: 10.1093/eurheartj/ehz455)

Randomized Comparison of Efficacy and Safety of Lipid Lowering With Statin Monotherapy Versus Statin-Ezetimibe Combination for High-Risk Cardiovascular Disease - RACING

Aug 05, 2022

Study Design

The **RACING** trial was a **multicenter, open-label trial** among 26 centers in South Korea.

Patients with documented atherosclerotic cardiovascular disease (ASCVD) were randomized in a 1:1 fashion to ezetimibe and moderate-intensity statin (rosuvastatin 10 mg with ezetimibe 10 mg once daily; **n = 1,894**) or high-intensity Statin monotherapy (rosuvastatin 20 mg once daily; **n = 1,886**).

Results were Analyzed in an intention-to-treat fashion.

Total randomized participants: 3,780

The median duration of follow-up: 3 years

Mean patient age: 64 years

Percentage female: 25%

Results

- ❖ The **results** of this trial show that, among patients with **ASCVD**, treatment with a **Moderate-intensity** statin and ezetimibe were non-inferior to treatment with a high-intensity statin with respect to the composite of cardiovascular death, major cardiovascular events, or nonfatal stroke at three years.
- ❖ This study shows that a **drug combination strategy** can be utilized to achieve reductions in LDL cholesterol.
- ❖ Importantly, patients with **moderate-intensity** statin and ezetimibe had lower rates of drug discontinuation or dose reduction than patients receiving high-intensity Statin. However, the study is limited by its open-labeled design, which may have impacted reporting of patient-adverse effects.

2022

Drug Design, Development and Therapy

Dovepress

open access to scientific and medical research

 Open Access Full Text Article

REVIEW

Combination Therapy of Ezetimibe and Rosuvastatin for Dyslipidemia: Current Insights

Maya R Chilbert ^{1,2}, Dylan VanDuyn ³, Sara Salah ¹, Collin M Clark ^{1,2}, Qing Ma ¹

¹Department of Pharmacy Practice, School of Pharmacy and Pharmaceutical Sciences, University at Buffalo, Buffalo, NY, USA; ²Department of Pharmacy, Buffalo General Medical Center, Buffalo, NY, USA; ³Department of Pharmacy, Buffalo Veterans Affairs Medical Center, Buffalo, NY, USA

Correspondence: Maya R Chilbert, Department of Pharmacy Practice, University at Buffalo School of Pharmacy and Pharmaceutical Sciences, 202 Pharmacy Building, Buffalo, NY, USA, Tel +1 716 829-5172, Fax +1 716-829-6093, Email mayahols@buffalo.edu

Study	Study design	N	Regimens	LDL- C Lowering (mg/dL)	Achieve LDL-C Goal (% of Patients)
EXPLORER14	This 6-week, open-label, randomized, parallel-group study	469	RSV/EZ 40 mg/10mg vs RSV 40 mg	RSV/EZ: 70.0a RSV: 57.0 p<0.001	RSV/EZ: 94.0% RSV: 79.1% p<0.001
Yang15	12-week, randomized, double-blind, placebo-controlled, multicenter study. A total of 337 patients were screened	337	RSV/EZ 5–20/10mg vs RSV 5–20mg	RSV/EZ: 59.5a RSV: 51.1 p<0.001	RSV/EZ: 90.7% RSV: 72.9% p=0.01
MRS-ROZE16	Multicenter eight-week randomized double-blind phase III study	407	RSV/EZ 5–20/10mg vs RSV 5–20mg	RSV/EZ: 59.1b RSV: 49.4 p<0.001	RSV/EZ: 94.1% RSV: 86.3% p<0.05
I-ROSETTE17	I-ROSETTE (ildong rosuvastatin & ezetimibe for hypercholesterolemia) was an 8-week, double-blind, multicenter, phase III randomized controlled trial	396	RSV/EZ 5–20/10mg vs RSV 5–20mg	RSV/EZ: 75.4a RSV: 64.4 p<0.001	RSV/EZ: 92.3% RSV: 79.9% p<0.001
Kim W18	Multicenter, randomized, double-blind study comprised a main study and an extension study.	712	RSV/EZ 5–20/10mg vs RSV 5–20mg	RSV/EZ: 56.5%c RSV: 45.2% p<0.01	RSV/EZ: 94.2% RSV: 86.6% P=0.014

24 May 2021

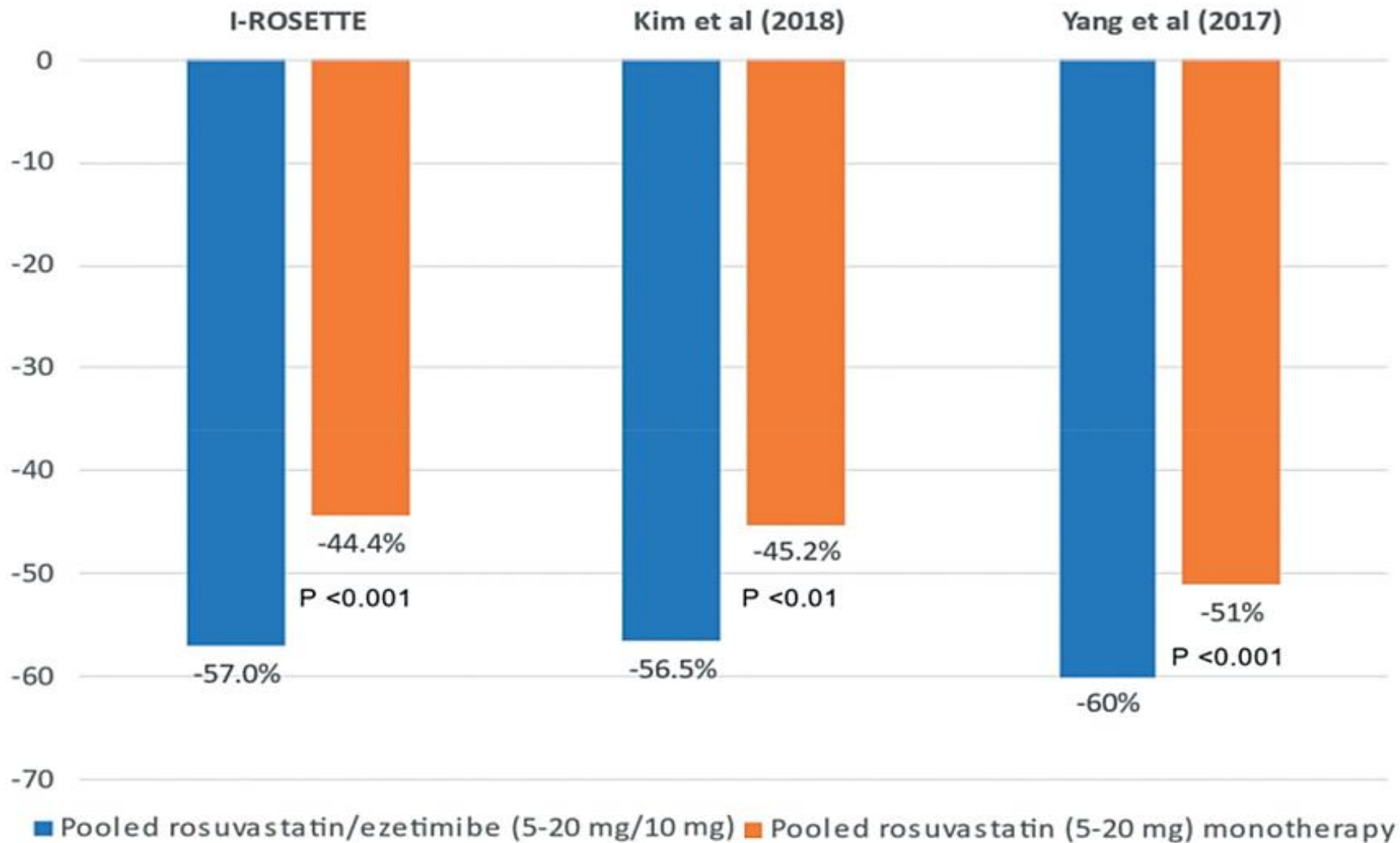


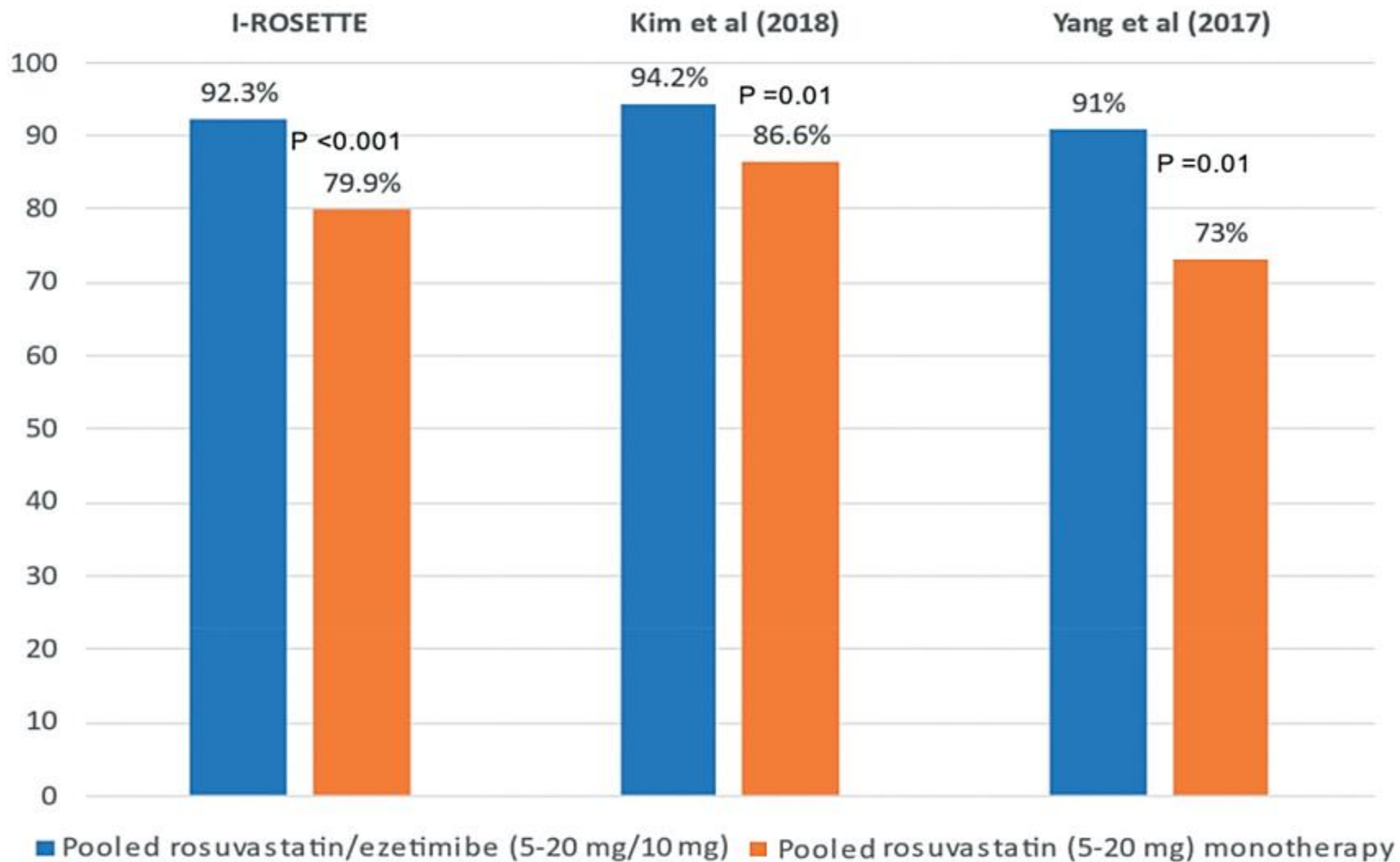
Expert Review of Clinical Pharmacology

ISSN: (Print) (Online) Journal homepage: <https://www.tandfonline.com/loi/ierj20>

Fixed-dose combination of rosuvastatin and ezetimibe: treating hypercholesteremia according to cardiovascular risk

Vivencio Barrios & Carlos Escobar





Result

- ❖ Many studies have shown that **up titrating statin doses** is less effective than adding ezetimibe, as combined therapy provides greater LDLC reductions without increasing the risk of adverse events, because of the complementary mechanisms of action.
- ❖ Of note, the combination of rosuvastatin and ezetimibe markedly reduces LDL-C levels (up to **60%-75%** from baseline), leading to the achievement of LDL-C goals in a broad spectrum of patients with hypercholesterolemia, along the cardiovascular risk continuum, including those with established atherosclerotic CVD .

Conclusion

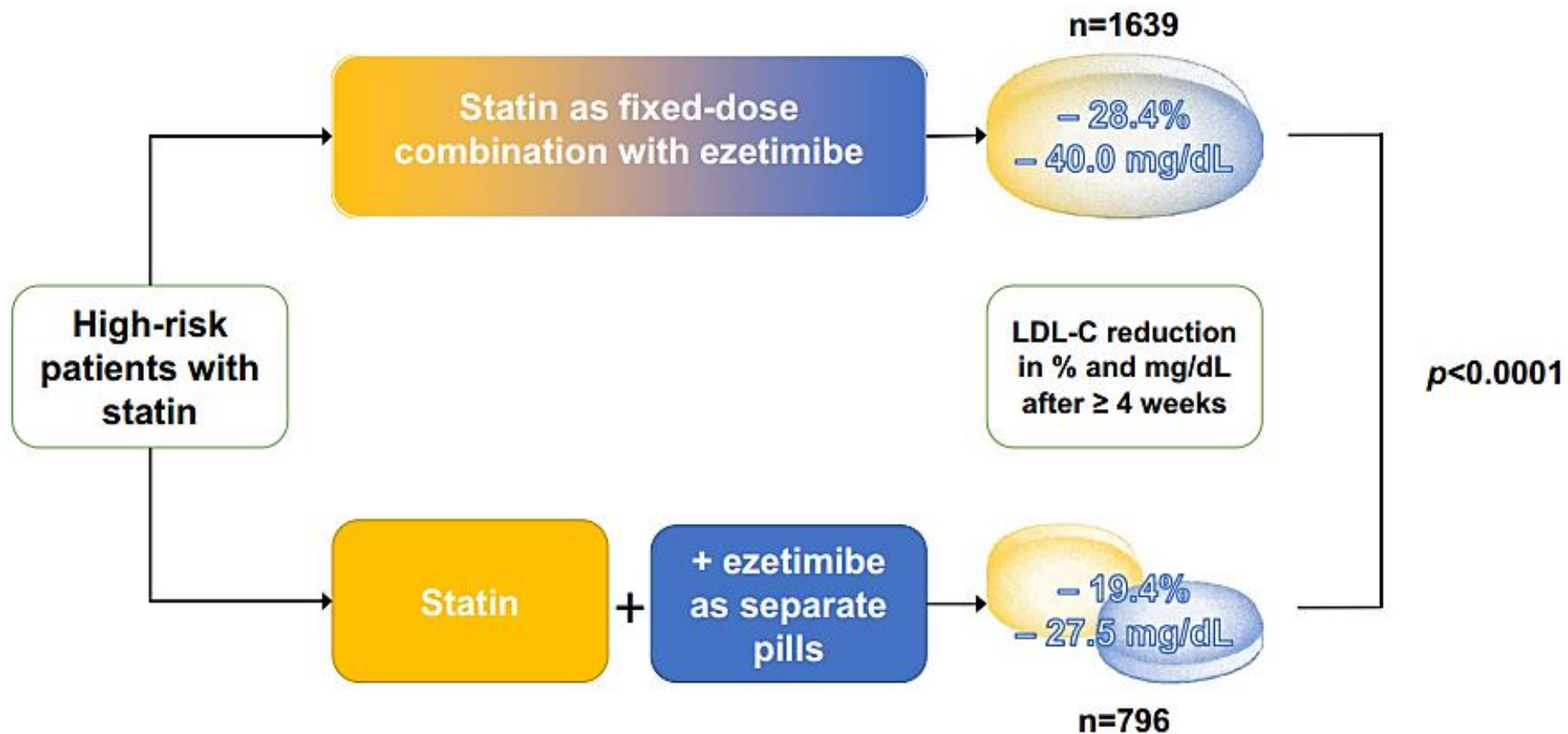
- The combination of rosuvastatin and ezetimibe provides important LDL-C reductions (**up to 60–75%**), with a good safety profile.
- Various clinical trials have demonstrated the beneficial effects of combining rosuvastatin with ezetimibe in a broad spectrum of patients with hypercholesterolemia, including those at **high risk** and those with **atherosclerotic CVD**.
- In addition, the fixed-dose combination may improve **medication adherence**, thus adding value in the treatment of these patients.



Non-statin lipid-lowering therapy over time in very-high-risk patients: effectiveness of fixed-dose statin/ezetimibe compared to separate pill combination on LDL-C

Julius L. Katzmann¹  · Francesc Sorio-Vilela² · Eugen Dornstauber³ · Uwe Fraas³ · Timo Smieszek⁴  · Sofia Zappacosta⁴ · Ulrich Laufs¹ 

Received: 26 May 2020 / Accepted: 3 September 2020
© The Author(s) 2020





ORIGINAL RESEARCH

Comparison of the Efficacy and Safety of Rosuvastatin/Ezetimibe Combination Therapy and Rosuvastatin Monotherapy on Lipoprotein in Patients With Type 2 Diabetes: Multicenter Randomized Controlled Study

Jiwoo Lee · You-Cheol Hwang · Woo Je Lee · Jong Chul Won ·

Kee-Ho Song · Cheol-Young Park · Kyu Jeung Ahn · Joong-Yeol Park

Received: December 12, 2019 / Published online: February 17, 2020
© The Author(s) 2020

Study design & Conclusion

Randomized, multicenter , open-label, parallel-group study, patients were randomly assigned to receive the combination therapy of rosuvastatin 5 mg/ezetimibe 10 mg once daily (n = 68) or monotherapy with rosuvastatin 10 mg once daily (n = 68), for 8 weeks.

An 8-week combination therapy of rosuvastatin 5 mg/ezetimibe 10 mg showed a significant **reduction in the apoB/A1 ratio**, a predictor of future cardiovascular disease, compared to rosuvastatin 10 mg monotherapy, in patients with **diabetes** and **hypercholesterolemia**. No unexpected safety issues were identified, and both treatments were well tolerated.

Comparison of the effect of rosuvastatin versus rosuvastatin/ezetimibe on markers of inflammation in patients with acute myocardial infarction

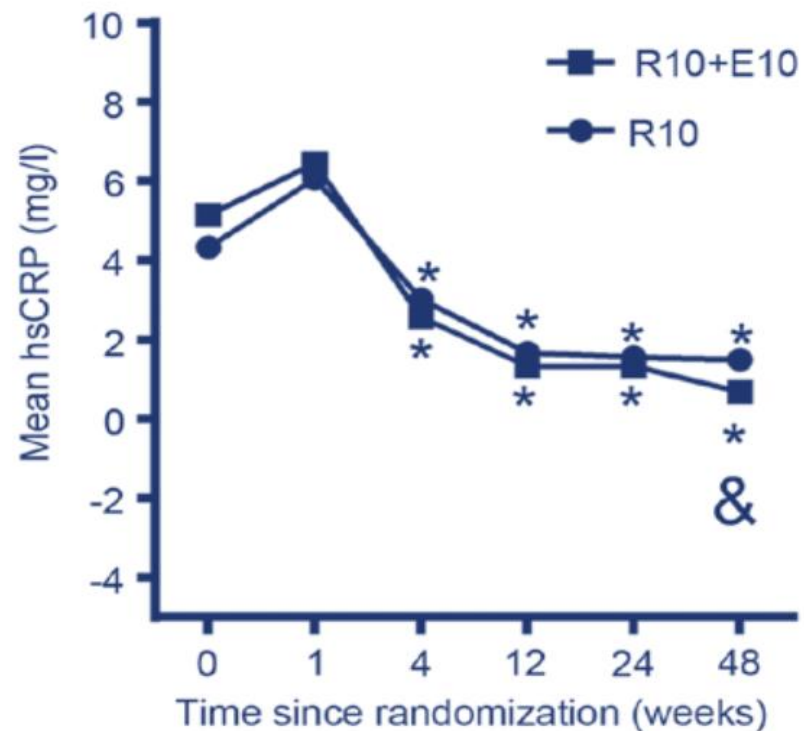
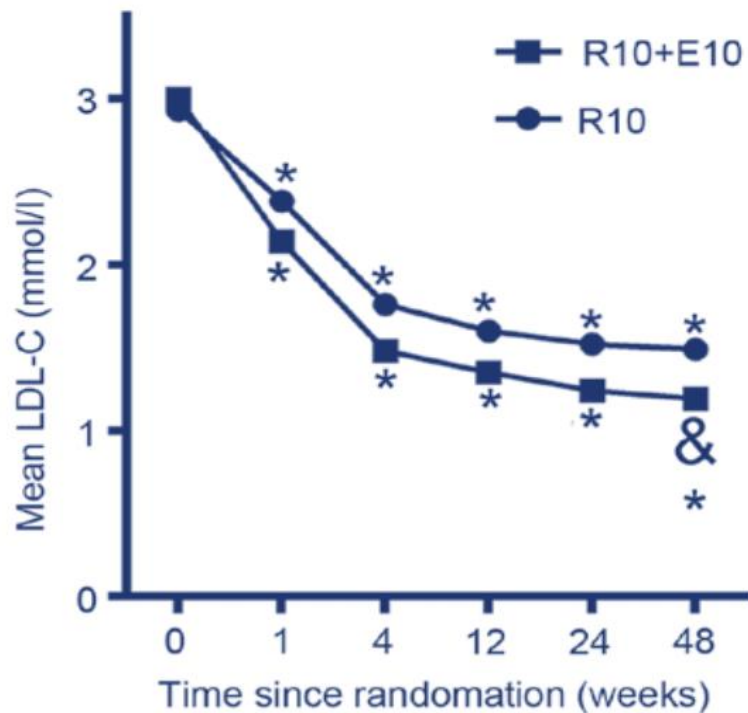
YIZHI REN¹, HAO ZHU^{1,2}, ZHONGGUO FAN¹, YALI GAO¹ and NAILIANG TIAN^{1,2}

¹Department of Cardiology, Nanjing First Hospital, Nanjing Medical University;

²Department of Cardiology, Nanjing Heart Center, Nanjing, Jiangsu 210006, P.R. China

Received October 5, 2016; Accepted June 22, 2017

LDL-C, Lp-PLA2 and hsCRP levels over time following randomized treatment



Conclusion

- The preset study confirmed that the addition of ezetimibe to rosuvastatin further **reduced LDL-C and hsCRP**, and also resulted in further **reductions in Lp-PLA2**, as compared with rosuvastatin monotherapy.
- The alterations in the levels of Lp-PLA2 were weakly but significantly correlated with LDL changes, which indicated that Lp-PLA2 reduction is only partly explained by LDL-C lowering.
- These findings provide evidence for the debate concerning the value of adjunctive LDL-C reduction in combination with a statin. In addition, reductions of Lp-PLA2 levels may be considered as target for the suppression of inflammation.

ARTICLE IN PRESS

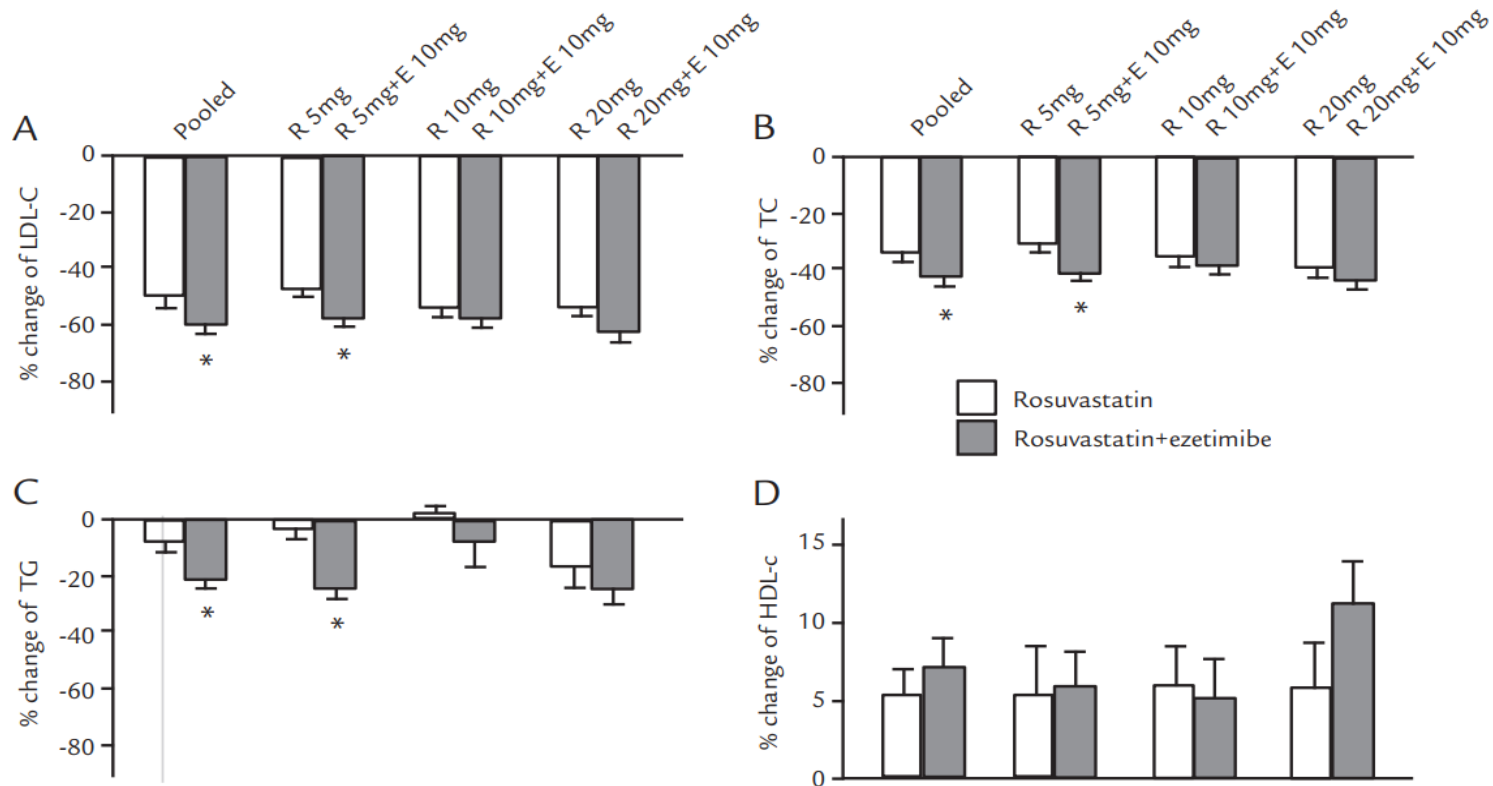
Clinical Therapeutics/Volume ■, Number ■, 2016

Combination Therapy of Rosuvastatin and Ezetimibe in Patients with High Cardiovascular Risk

A 12-week (4 weeks of lifestyle changes and 8 weeks of drug treatment), randomized, double-blind, placebo-controlled, multicenter study conducted at 28 sites in Korea.

CONCLUSION & Result

The results indicate that **rosuvastatin/ezetimibe** combination therapy has better efficacy than rosuvastatin monotherapy. Specifically, the combination therapy **lowered LDL-C to -63% and achieved the LDL-C target in 91% of Koreans with high cardiovascular risk.**



-
- ✓ درمان مونوتراپی چند درصد بیماران را به تارگت LDL می‌رساند ؟
 - ✓ در صورت نرسیدن به تارگت درمان ، ترجیح افزایش دوز استاتین است یا اضافه کردن Ezetimibe و استفاده از ترکیب Statin/Ezetimibe ؟
 - ✓ به چه عللی ممکن است اضافه کردن Ezetimibe به Statin به مونوتراپی استاتین ترجیح داده شود؟
 - ✓ بر اساس مقالات و گایدلاینهای اخیر که نشاندهنده این است که ترکیب Rosuvastatin/Ezetimibe نسبت به Rosuvastatin به تنهایی Cardiovascular Events را بیشتر کاهش میدهد، چند درصد نسخ از مونوتراپی statin به ترکیب Rosuvastatin/Ezetimibe شیفتمی کند؟

 Thank You
For Your Attention



No. 58, 8th St., Kooye Nasr (Gisha St.),
Tehran, IR Iran, Postal Code: 1446863914
Telefax: +98 (21) 41637000

www.actoverco.com



Together for a healthy future