



**Chelfi Zhi Fei Chua<sup>1</sup>, Jing Fen Kho<sup>1</sup>**

<sup>1</sup> Sarawak Heart Centre

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## Introduction

Dyslipidemia is identified as one of the risk factors of cardiovascular disease. The prevalence of hypercholesterolemia has increased by 46% over 4 years, since 2011. Medications such as statins and ezetimibe have been used to manage dyslipidemia. For patients with poorly controlled dyslipidemia with existing medication, the prescribers can either increase the dose of current agent, switch to a different drug, or add on a different drug.

## Objectives

- 1) To analyse the pattern of use of rosuvastatin and ezetimibe in patients with poorly managed dyslipidemia.
- 2) To compare the effect of rosuvastatin alone versus add-on ezetimibe to atorvastatin in reducing total cholesterol (TC) and low-density lipoprotein-cholesterol (LDL-C).

## Methods

This study was conducted as a retrospective, observational study.

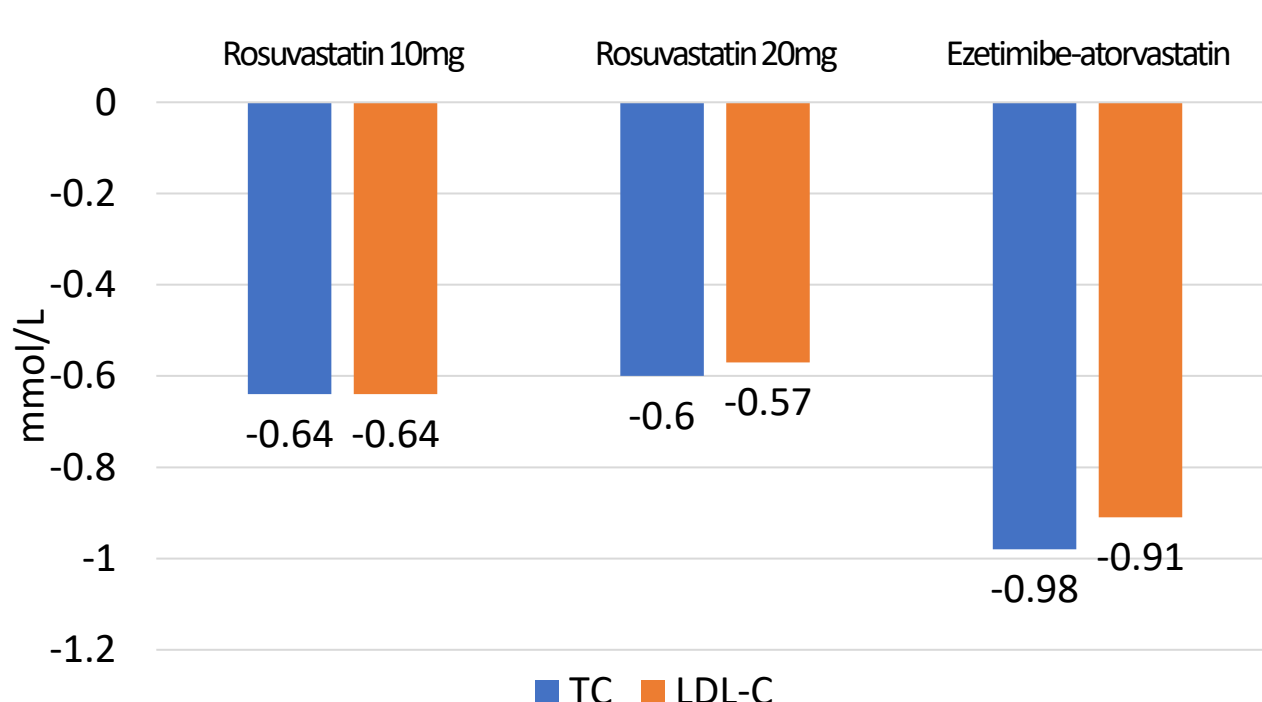
The domain of this study includes patients with newly introduced rosuvastatin to replace atorvastatin and patients with added ezetimibe to existing atorvastatin. The study period was started from 1<sup>st</sup> January 2018 to 30<sup>th</sup> June 2019. The baseline atorvastatin dose was set as 40mg ON, as this is the commonly prescribed dose for hypercholesterolemia patients with established CHD. Subjects were recruited from cardiac, cardiothoracic and heart failure clinics. All research data was retrieved from hospital medical record systems "Fisicien" and "e-Delphyn". Data analysis was then performed using Statistical Package for the Social Sciences version 26.

**Table 1** Demographic Data of Subjects

Characteristic	Rosuvastatin 10mg	Rosuvastatin 20mg	Ezetimibe-atorvastatin
Number of subjects	31	128	69
Sex			
Male (%)	23 (74.2)	110 (85.9)	56 (81.2)
Female (%)	8 (25.8)	18 (14.1)	13 (18.8)
Age Group (years)			
18-30 (%)	0 (0)	1 (0.8)	0 (0)
31-40 (%)	1 (3.2)	5 (3.9)	4 (5.8)
41-50 (%)	4 (12.9)	20 (15.6)	12 (17.4)
51-60 (%)	6 (19.4)	35 (27.3)	20 (29.0)
61-70 (%)	11 (35.5)	42 (32.8)	21 (30.4)
71-80 (%)	9 (29.0)	19 (14.8)	11 (15.9)
> 80 (%)	0 (0)	6 (4.7)	1 (1.4)
Race			
Malay (%)	6 (19.4)	46 (35.9)	25 (36.2)
Chinese (%)	15 (48.4)	50 (39.1)	29 (42.0)
Indian (%)	0 (0)	1 (0.8)	0 (0)
Sarawak Dayak (%)	9 (29.0)	31 (24.2)	14 (20.3)
Non-Malaysian (%)	1 (3.2)	0 (0)	1 (1.4)
Mean baseline lipid profile (mmol/L)			
TC (SD)	5.38 (0.97)	4.91 (1.05)	5.12 (1.11)
LDL-C (SD)	3.48 (0.76)	3.07 (0.88)	3.21 (1.03)

Abbreviations: TC, total cholesterol; LDL-C, low-density lipoprotein-cholesterol; SD, standard deviation

**Figure 1** Mean Changes of TC and LDL-C



## Results

A total of 228 patients were recruited in this study. There were 31 subjects (13.6%) in rosuvastatin 10mg arm, 128 (56.1%) in rosuvastatin 20mg arm, and 69 (30.3%) in ezetimibe-atorvastatin arm.

The findings of the study showed that the mean reduction of TC and LDL-C for all subjects were  $0.721 \pm 0.987$  mmol/L and  $0.685 \pm 0.913$  mmol/L respectively.

The mean TC reduction was the greatest in ezetimibe-atorvastatin arm, with mean of  $0.978 \pm 0.93$  mmol/L, followed by  $0.64 \pm 1.11$  mmol/L in rosuvastatin 10mg arm, and  $0.60 \pm 0.97$  mmol/L in rosuvastatin 20mg arm.

The pattern of LDL-C reduction in three arms was similar to TC reduction. Ezetimibe-atorvastatin showed the greatest reduction in LDL-C with mean of  $0.91 \pm 0.81$  mmol/L, followed by  $0.64 \pm 0.97$  mmol/L in rosuvastatin 10mg, and  $0.57 \pm 0.94$  mmol/L in rosuvastatin 20mg.

TC reduction was statistically significantly lower in ezetimibe-atorvastatin group compared to rosuvastatin 20mg group ( $p=0.029$ ). There was no statistically significant difference in TC reduction between rosuvastatin 10mg and 20mg arms ( $p=0.99$ ) as well as between ezetimibe-atorvastatin and rosuvastatin 10mg arms ( $p=0.24$ ).

LDL-C reduction was also statistically significantly lower in ezetimibe-atorvastatin group compared to rosuvastatin 20mg arm ( $p=0.036$ ). Difference in LDL-C reduction was non-significant between rosuvastatin 10mg and 20mg ( $p=0.926$ ), and between ezetimibe-atorvastatin and rosuvastatin 10mg arm ( $p=0.358$ ).

The findings were in line with results published by Foody et al. Foody et al. noted that addition of ezetimibe to statin offered a better control of LDL-C than statin monotherapy. Ezetimibe-statin arm showed larger proportion of subjects achieving LDL-C target.

This study has a few limitations, the major one being the assessment of adherence to medical therapy. This study does not account for patient's adherence to medications. Lifestyle issues such as diet, exercise, smoking status are not considered in the project as well. Comorbidities, such as, diabetes, hypertension, and familial hypercholesterolemia are not taken into account as well. These factors may affect the control of cholesterol level in this project.

## Conclusion

Use of ezetimibe and atorvastatin or switching of atorvastatin to rosuvastatin managed to reduce TC and LDL-C levels in patients with poorly managed dyslipidemia despite on atorvastatin. Ezetimibe-atorvastatin showed greater reduction in TC and LDL-C compared to rosuvastatin.

## References

1. Ministry of Health Malaysia (2017) *Management of dyslipidemia* 5<sup>th</sup> Edition of Clinical Practice Guidelines.
2. Foody J.M., Toth P.P, Tomassini J.E., Sajjan S., Ramey D.R., Neff D., Tershakovec A.M., Hu H., Tunceli K. (2013) *Changes in LDL-C levels and goal attainment associated with addition of ezetimibe to simvastatin, atorvastatin, or rosuvastatin compared with titrating statin monotherapy* *Vascular Health and Risk Management* 9:719-727.