

# Addressing the unmet need of high-risk cholesterol patients

By **Laxmi Iyer** - March 13, 2017

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*A recent Dyslipidemia International Study (DYSIS), which was carried out in Asia Pacific countries including four hospitals in Singapore, revealed that a large percentage of local patients with existing heart diseases were unable to lower their "bad" cholesterol levels (LDL cholesterol) despite diet, exercise and therapy with a single moderate-intensity statin. These results were presented at the Singapore Cardiac Society's most recent Annual Scientific Meeting.*

*The Dyslipidemia International Study (DYSIS), which was carried out in thirty countries worldwide, looked at the level of low-density lipoprotein cholesterol (LDL-C) target attainment in patients on lipid-lowering therapy. DYSIS II, which was also carried out in Singapore, studied LDL-C targets achievement in patients with acute coronary syndrome (ACS) and stable coronary heart disease (CHD).*

*In conversation with Biotechn.Asia, **Associate Professor Dr Poh Kian Keong**, who was one of the investigators of DYSIS and Clinical Director of Research, Department of Cardiology, National University Heart Centre (NUHCS), comments on the results of DYSIS and what this means for patients in Singapore. **Dr Peter Yan Chee Hong**, Consultant Cardiologist and Physician at Gleneagles and Mount Elizabeth Hospitals, speaks about the unmet need of high-risk patients and the role of combination statins*



*Prof Poh Kian Keong*

**Associate Professor Poh Kian Keong, Senior Consultant, Department of Cardiology, National University Heart Centre Singapore**

**What is dyslipidemia and what are the risks associated with it?**

Dyslipidemia refers to abnormal plasma lipid, including LDL-C, HDL, TG levels. Very often, the lipid levels are high (hyperlipidemia). Atherogenic dyslipidemia is one of the major risk factors that contribute to increased risk of developing cardiovascular diseases, in particular, coronary heart diseases.

**What was DYSIS about?**

The Dyslipidemia International Study (DYSIS) is a prospective, cross-sectional registry documenting lipid profiles in patients at both inpatient and outpatient settings with various risk levels (very high risk, high risk and non-high risk) throughout 30 countries on a global scale (across Europe, the Middle East, Africa, and Asia). DYSIS was aimed at determining treatment target attainment globally using standardized data collection.

**Which countries in Asia were involved in the study and how did their results compare against the global findings?**

Besides Singapore, countries such as Hong Kong, India, Indonesia, Philippines, South Korea, Taiwan, Thailand, and Vietnam are involved in the study.

Though the exact level of LDL-C target attainment varied across countries, overall the results are consistent in that only about 30% of acute coronary syndrome (ACS) and stable coronary heart disease (CHD) patients achieved their LDL-C target.

## **What do the findings of DYSIS mean for physicians and patients in Asia?**

The findings of DYSIS have demonstrated that LDL-C values for very high risk patients were far from desired target goal despite moderate-intensity statin monotherapy. This calls for more effective lipid lowering therapies, such as combination therapy in order to improve patients' outcomes, particularly the very high-risk cohort.

### **Dr Peter Yan Chee Hong, Consultant Cardiologist and Physician, Gleneagles and Mount Elizabeth Hospitals**

**As a practicing physician, what are some of the challenges that you have identified in high-risk patients who have been unable to lower their cholesterol levels?**

Challenges in bringing the LDL level to target international recommendations for high-risk patients have been difficult to achieve because of the high standards of lowering LDL to levels in the region of below 70 mg/dl. Monotherapy with statins will require high dose (high intensity) statins to be able to achieve the LDL goal target. In other words, doses of statins for atorvastatin between 40 to 80 mg and rosuvastatin between 20 to 40 mg. These high doses (i.e. high intensity) statins however, are not well-tolerated in the Asian patients. High-dose statins carry with it numerous side effects which include:



*Dr Peter Yan*

1. Muscle pain (myalgia)
2. Muscle inflammation (myositis)
3. Liver dysfunction (transaminitis, i.e. elevation of liver enzymes)
4. Reportedly fear of increased dementia, incidence of diabetes mellitus and cataracts

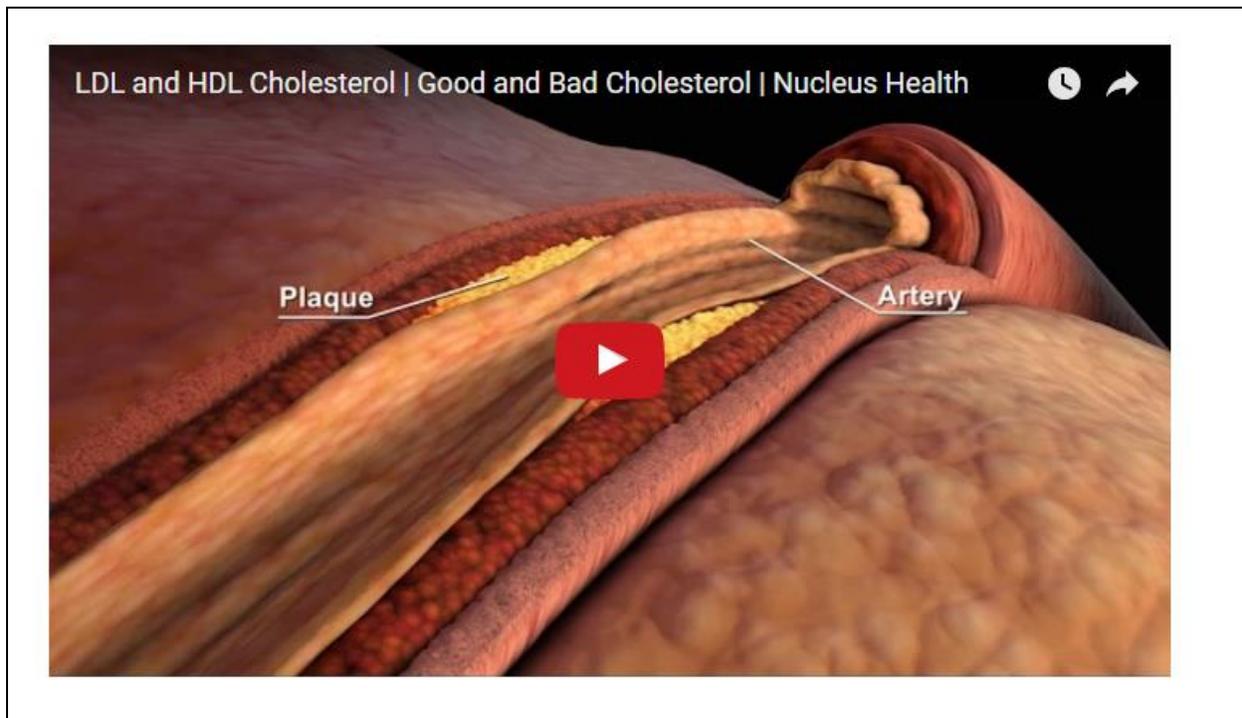
The above side effects have been over-emphasised and the internet is filled with caution on the use of statins. As a result, patients develop phobia over the use of high-intensity statins and would rather not be on this kind of doses. Studies in Singapore have shown that only low to moderate-dose intensity statins are used in high-risk patients and as a result, a majority (over 70%) of high-risk patients are not treated to the LDL goal targets.

Furthermore, there is also the doctors' reluctance (doctor phobia) to titrate the dose of statins to high intensity for the same caution on the side effects.

**Why is there a need for a combination statin? How does it differ from statin monotherapy?**

In view of the above, there is a need for an alternative therapy for achieving the LDL goal targets in these high-risk patients. A good drug for this is ezetimibe (a cholesterol absorption inhibitor) which is able to, in combination with a statin, reduce the LDL further by 18 to 20%. Usually when we double the dose of a monotherapy statin, the additional LDL reduction achievable is only about 6%. Therefore, the addition of ezetimibe to low to moderate dose statins would be able to reduce the LDL level by another 18 to 20%. Moreover, not every individual responds to the same dose of statins with the same reduction of LDL levels. There is marked individual variability on a single fixed statin dose. Many will also not achieve the LDL target even on high-dose statins and therefore combination of the most tolerable dose of statins with ezetimibe again may be able to achieve the LDL goal targets.

*Recently, Singapore's Health Sciences Authority announced the approval of **ATOZET®** to treat patients who are unable to control their cholesterol levels with a single statin alone. ATOZET® which is a combination of two statins – ezetimibe and atorvastatin – has been clinically proven to lower cholesterol levels significantly than doubling the dose of atorvastatin.*



### **FULL TEXT**

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