Medical *Education* Network

PRIORITY PRESS

79th European Atherosclerosis Society (EAS) Congress

Gothenburg, Sweden / June 26-29, 2011

Achieving Lipid Goals in Patients at Risk of Cardiovascular Disease: Joint EAS/ESC Guidelines

Gothenburg - As presented here at the EAS congress, the first guidelines for the management of dyslipidemias—produced jointly by the European Atherosclerosis Society (EAS) and the European Society of Cardiology (ESC)—stress LDL–C as the primary target of therapy and set goals for LDL-C lowering in patients at very high, high and moderate risk of cardiovascular disease. Although the guidelines do not make recommendations for individual statins, they stress the need to use an effective dose to achieve the appropriate LDL-C goal. Studies of LDL-C goal achievement in high-risk patients showed the need for high-dose treatment in these groups. The efficacy and safety of statins in patients also receiving antiplatelet therapy and a study on the patterns of antiplatelet/antithrombotic therapy in patients with acute coronary syndromes were also highlighted at the congress.

Chief Medical Editor: Dr. Julie Frère, Montreal, Québec

The highlight of the European Atherosclerosis Society (EAS) congress was the launch and simultaneous publication of the first joint European Society of Cardiology (ESC)/EAS guidelines for the management of dyslipidemia (Catapano et al. *Atherosclerosis* 2011; 217S:S1–S44, Reiner et al. *Eur Heart J* 2011;32:1769-818, also available on the ESC website at www.esccardio.org). Lead EAS author Prof. Alberico Catapano, Department of Pharmacological Science, University of Milan, Italy, stressed that LDL-C is the primary target of therapy. Every 1.0 mmol/L (40 mg/dL) reduction in LDL-C is associated with a corresponding 22% reduction in cardiovascular (CV) mortality and morbidity, he noted. The guidelines set the goal for LDL-C lowering in patients at very high CV risk at <1.8 mmol/L (<70 mg/dL) or a ≥50% reduction from baseline LDL-C (European guidelines use 4 levels of risk stratification based on SCORE which distinguishes very high risk from high risk vs. high, medium and low risk based on Framingham Risk Scores used in Canada). In the majority of patients, this is achievable with statin monotherapy, as noted in the new guidelines. In high-risk and moderate-risk patients, LDL-C goals are <2.5 mmol/L (<100 mg/dL) and <3 mmol/L (<115 mg/dL), respectively "There is no doubt that a statin is the first choice for lowering LDL-C," Prof. Catapano told delegates. Although the guidelines do not differentiate between individual statins, an addendum (Reiner et al. *Eur Heart J* 2011 doi:10.1093/eurheartj/ehr169) provides a table for assessment of the percentage reduction in LDL-C required to achieve goals based on the starting LDL-C value. Once this has been determined, the treatments that can help in reaching that goal can be identified.

Invited commentator Dr. W. Virgil Brown, Emory University School of Medicine, Atlanta, Georgia, questioned whether the guidelines were aggressive enough in setting LDL-C goals, citing the case of Canadian Cholesterol guidelines which set a goal of <2 mmol/L (<77 mg/dL) in moderate-risk patients (Genest et al. *Can J Cardiol* 2009;25:567-79). "Unlike blood pressure and blood glucose, we have never found a problem in lowering LDL-C—there is no lower limit," he declared.

Achieving LDL-C Goals in High-risk Patients

The benefits of using rosuvastatin over atorvastatin at approved doses to lower LDL-C in high-risk patients were demonstrated in 2 studies presented here at the congress. Both studies used data from VOYAGER meta-analysis. The VOYAGER database included 32,258 patients from 37 studies involving fixed-dose comparisons of rosuvastatin with either atorvastatin or simvastatin.

One study looked at goal achievement to <70 mg/dL (<1.8 mmol/L) in the 8859 patients diagnosed with diabetes mellitus. The percentage of these patients achieving goal rose as the dose of statin increased, reported clinical researcher Dr. Björn W. Karlson, Mölndal, Sweden. Rosuvastatin appeared more efficacious than atorvastatin in lowering LDL-C, with 28.9% to 53.3% of patients receiving rosuvastatin 10 to 40 mg achieving goal compared with 10.2% to 33.8% of patients receiving atorvastatin 10 to 80 mg. The differences were statistically significant between rosuvastatin vs. atorvastatin at a 1:1 and 1:2 dose comparison (P<0.001). "When we classified patients according to baseline LDL-C <130, ≥130-<160 and ≥160 mg/dL (<3.4-≥4.1 mmol/L), we found that goal attainment was higher in the patients with lowest LDL-C at the start of treatment," Dr. Karlson reported. "The message is that you should use a good statin and you should titrate." In all 3 groups, the rate of patients achieving goal was higher in the patients taking rosuvastatin, he added.

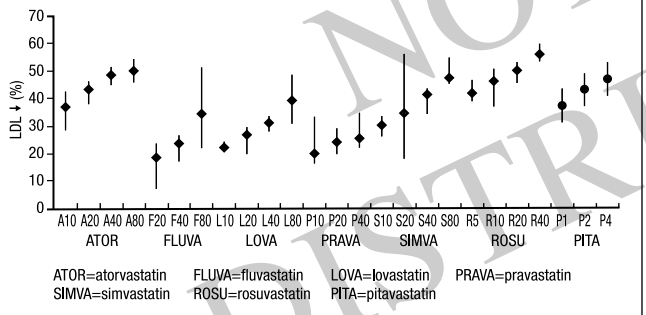
The second study observed 4685 high-risk VOYAGER patients who had high baseline LDL-C plus either diabetes, atherosclerotic disease or elevated triglycerides in combination

Continued

with low HDL-C. Improvements in LDL-C levels were again seen with increasing doses of both statins, but there were statistically significant differences in percentage change in LDL-C from baseline in favour of rosuvastatin. A higher percentage of patients with baseline LDL-C ≥160 mg/dL (≥4.1 mmol/L) achieved LDL-C goals of <100 mg/dL (<2.6 mmol/L) and <70 mg/dL (<1.8 mmol/L). "Achieving both goals was quite difficult with low doses of either statin in these patients, but increasing the dose increased percentages up to 40% for the lower goal and up to 60 to 70% for the easier goal. Once again, the message is that you should use an effective high-dose statin and you should titrate to a reasonable dose in these high-risk patients," Dr. Karlson stated. He added that the results of both these studies were consistent with those in the overall VOYAGER population (Nicholls et al. *Am J Cardiol* 2010;105:69-76).

Rosuvastatin also produced a dose-related increase in HDL-C, ranging from 3.6% with the 5-mg dose to 9.2% with the 40-mg dose. Dr. Karlson told delegates that more information about this effect might emerge from the SATURN trial (Nicholls et al. *Curr Med Res Opin* 2011;27:1119-29), the results of which are expected later this year. "We will see whether the difference between the effects of rosuvastatin 40 mg and atorvastatin 80 mg on HDL-C is reflected in the effect on atherosclerosis regression as imaged by intravascular ultrasound," he noted.

Figure 1. **A Systematic Review of the Therapeutic Equivalence of Statins**



Adapted from Reiner et al. *Eur Heart J* 2011 doi:10.1093/eurheartj/ehr169.

Antiplatelet Therapy Co-Administration

Questions have been raised about the potential for interaction between the antiplatelet agent clopidogrel and atorvastatin, as both drugs are metabolized by cytochrome P450 3A4 (CYP3A4). Dr. Jung-Won Suh, Seoul National University Bundang Hospital, South Korea, reported here at the EAS on a study of atorvastatin and rosuvastatin, which is not metabolized by CYP3A4, showing that neither drug reduced the efficacy of antiplatelet regimens.

Dr. Suh and her colleagues carried out a post-hoc analysis of 915 patients who underwent coronary intervention with drug-eluting stents (DES) in the CILON-T trial (Suh et al. *J Am Coll Cardiol* 2011;57:280-9). Patients were randomized to receive either dual antiplatelet therapy (ASA and clopidogrel) or triple antiplatelet therapy (ASA, clopidogrel and cilostazol) for 6 months. They also received atorvastatin 20 mg/day or rosuvastatin 10 mg/day. "After 6 months, we saw no statistically significant differences in platelet inhibition between the statin groups," Dr. Suh reported. "We concluded that there is no loss of efficacy with atorvastatin in DES patients on antiplatelet therapy with clopidogrel, with or without cilostazol, which is also metabolized by CYP3A4." She added that patients on rosuvastatin achieved significantly lower LDL-C than patients on atorvastatin, irrespective of the type of antiplatelet therapy (mean 64.9 vs. 68.8 mg/dL, P=0.02).

EPICOR: Antithrombotic Management Patterns in ACS

A new international observational study that aims to provide a representative reflection of real-life management of acute coronary syndromes (ACS) with pharmacological therapies and invasive strategies was described here at the EAS by Dr. Héctor Bueno, Hospital General Universitario Gregorio Marañón, Madrid, Spain, and multicentre European colleagues. The EPICOR study will document clinical and economic outcomes of short- and long-term antithrombotic management patterns (AMPs) and compare them between hospitals, countries and regions. The trial has enrolled a total of 10,569 adults hospitalized with ACS (unstable angina or myocardial infarction [STEMI or NSTEMI]) at approximately 700 centres in 21 countries in Europe and Latin America. In-hospital information will be provided by local staff, while centralized follow-up will be performed at a country level through telephone calls using standardized questionnaires, with subsequent validation of outcomes by physician interviews. The primary end point of the study is the rate of clinical outcomes (ischemic and hemorrhagic) associated with the most frequent AMPs used for ACS treatment. Dr. Bueno and co-investigators announced that in-hospital results should be available late 2011, with 6-month data expected in 2012. □

To view an electronic version of this publication along with related slides if available, please visit www.mednet.ca/2011/pp12-008e.

Medical Education Network Canada Inc. 132 chemin de l'Anse, Vaudreuil, Quebec J7V 8P3

PP12-008E ML