Re: D Dulay, SA LaHaye, KA Lahey, AG Day. Efficacy of alternate day versus daily dosing of rosuvastatin. Can J Cardiol 2009;25(2):e28-e31.

To the Editor:

Alternate day dosing of rosuvastatin: Potential usefulness in statin-intolerant patients

We commend Dulay et al (1) for their well-designed crossover trial of the efficacy of 20 mg alternate day versus 10 mg daily dosing of rosuvastatin on low-density lipoprotein cholesterol (LDL-C) lowering. In particular, they noted a 48.5% versus 40.9% LDL-C reduction with daily versus alternate day rosuvastatin dosing, respectively. Despite the additional absolute LDL-C reduction of 7.6% with the daily dosing regimen, Dulay et al (1) stated the alternate day regimen was associated with a minimum 37.5% cost savings compared with daily dosing. Thus, a primary conclusion of their study was that alternate day dosing may represent an affordable yet efficacious approach for financially constrained individuals.

Another important barrier to statin adherence is tolerability. Myopathy, ranging from common myalgias to rare but life-threatening rhabdomyolysis, represents an important cause of statin discontinuation in clinical practice. Although the incidence of statin myopathy is low (approximately 1.5% to 5.0%) in randomized clinical trials (2,3), several observational studies (4,5) have demonstrated higher incidences of approximately 5% to 10%.

Both atorvastatin and rosuvastatin have relatively long plasma half-lives (6), making them potential candidates for consideration of alternate day dosing regimens, with the possible further benefit of reduced exposure to side effects. Although not specifically tested in statin-intolerant patients, a double-blind, placebo-controlled trial in 35 patients taking 10 mg atorvastatin daily versus 10 mg atorvastatin on alternate days showed LDL-C reductions of 38% and 35%, respectively, with no development of adverse symptoms (7). A retrospective analysis of our own patients (n=7) treated with 5 mg or 10 mg alternate day dosing of rosuvastatin revealed an LDL-C reduction of 25.9% and 37.9%, respectively (unpublished observations). In 51 previously statin-intolerant patients, alternate day dosing of rosuvastatin at 5 mg or 10 mg (mean 5.6 mg/day) resulted in a mean LDL-C reduction of 34.5% after a mean of 4.6 months. Importantly, 80% of patients had no recurrence of their myalgias (8). Even once to three times weekly rosuvastatin dosing regimens have demonstrated LDL-C reductions ranging from 20% to 38% among individuals with previous statin intolerance (9,10). Among our own patients on a three times weekly regimen of either 5 mg or 10 mg of rosuvastatin (n=6, mean dose 22.5 mg/week), an LDL-C reduction of 27.6% was achieved (unpublished observations). Thus, alternate day dosing regimens of rosuvastatin may be a practical alternative based on cost considerations but also due to tolerability, particularly among individuals with previous statin intolerance. However, the efficacy of alternating day statin regimens on cardiovascular disease outcomes remains to be evaluated.

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CONFLICTS OF INTEREST: Dr RA Hegele (Advisory Boards and Speakers Bureaus: Pfizer, Merck Frosst, Schering, AstraZeneca, Boehringer Ingelheim, Solvay and Kowa). Dr T Joy (Speakers Bureaus: Merck Frosst, Schering).

Tisha Joy MD FRCPC,
Robert A Hegele MD FRCPC FACP
Robarts Research Institute,
Schulich School of Medicine and Dentistry,
University of Western Ontario,
London, Ontario

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Editor's Note:
This letter was forwarded to the authors of the paper in question but no response was received.