

Australians launch trial to investigate statin's effect on AMD progression

Cheryl Guttman
in Fort Lauderdale, Florida

THE Age-related Maculopathy Statins Study (ARMSS) is now underway in Australia to investigate whether treatment with the HMG Co-A reductase inhibitor simvastatin (Zocor, Merck) can slow the progression of age-related macular degeneration, said Robyn H. Guymer MD, PhD, Centre for Eye Research, University of Melbourne, Australia.

“There have been no randomised, controlled trials looking at the relationship between cholesterol-lowering medications and AMD,”

The ARMSS will enroll 300 patients with high-risk fundus changes and will follow them for three years after randomisation to treatment with simvastatin 40 mg daily or placebo. Speaking at the annual meeting of the Association for Research in Vision and Ophthalmology, Dr Guymer described the rationale for the study and its design. She also urged colleagues to help in evaluating the question of how

statins may influence AMD. “There have been no randomised, controlled trials looking at the relationship between cholesterol-lowering medications and AMD, and results from available retrospective, cross-sectional, and longitudinal population-based studies have been contradictory. The ARMSS will provide us with information that is currently lacking regarding the efficacy of statins in AMD and we encourage others to also start gathering evidence now,” she said.

Dr Guymer pointed out that it may become much more difficult in the future to conduct and recruit patients for a placebo-controlled trial. Statins are already widely prescribed in the treatment of cardiovascular disease and strokes. Data is also accumulating to support their potential benefits for Alzheimer's disease, multiple sclerosis, diabetes, and increasing longevity.

Findings of previous studies contradictory

In the past five years there have been nine publications evaluating the relationship between AMD and treatment with cholesterol-lowering medications, including six looking specifically at statins. Six of the nine published studies showed some protective effect, whereas no benefit or an increased risk of AMD with cholesterol-lowering treatment was reported in others.

“Considering that cardiovascular disease and the cardiovascular risk factors for which patients are put on statins have been associated with AMD, it is not surprising that some studies found an association between AMD and statin use,” Dr Guymer observed.

There are many potential mechanisms by which statins might protect against AMD development and progression. Based on their effects on lipids, the statins may be expected to influence Bruch's membrane lipid deposition. However, the effects of statins are pleiotropic and these drugs may affect AMD through a variety of non-lipid related effects involving their vasodilatory, antiproliferative, anti-angiogenic, antioxidant, and anti-inflammatory properties. In addition, they may modulate resistance to complement through up-

regulation of complement inhibitor proteins.

“That latter activity is very interesting considering the recent finding of the association between the complement factor H gene and AMD,” Dr Guymer said.

The ARMSS is enrolling subjects with visual acuity better than 6/18 and high risk AMD defined as at least five drusen larger than 125 microns in both eyes, or one eye with end-stage AMD and the other with signs of early AMD. Fundus photograting is being performed at baseline and semi-annually to document progression or regression of AMD using a six category grading system. Study evaluations also include visual function tests of rod and cone function (flicker sensitivity, colour thresholds, dark adaptation curves).

“Since it is a small study, we chose to see if we could find some evidence of a benefit by looking at progression to higher risk levels of AMD. However, we are performing the visual function tests with the hope of finding some biomarker or other earlier indication of a positive effect,” Dr Guymer said.

Eligible patients must also have a normal cholesterol level, which for the purpose of the study is defined as any patient not currently receiving a cholesterol-lowering medication according to

Australian government eligibility guidelines for subsidised statin treatment. To avoid confounding of results from the visual function tests, patients with diabetes, glaucoma, or cataract are excluded.

Recruitment has been somewhat slow. Currently, 85 subjects have been enrolled and 50 have reached the 12-month visit. The trial has not been unmasked, but analyses performed so far show a significant decrease in cholesterol level in one treatment group. One patient in each treatment group has progressed to end stage disease, and most patients have demonstrated no change on their visual function tests while the rest show a mix of improvement and worsening.

The ARMSS study's investigators will obtain drug and placebo from Merck but has no other financial interest in the trial.

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