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Foreword

This supplement updates the current knowledge about the widely prescribed, synthetic HMG-CoA reductase inhibitor atorvastatin. In a series of six review articles, the supplement provides a comprehensive appraisal of the pharmacology, clinical efficacy and tolerability profile of atorvastatin in the treatment of hypercholesterolaemia and in the primary and secondary prevention of cardiovascular events.

Statins have now been available for approximately 20 years and have a prominent role in cardiovascular medicine, not only because they can achieve marked reductions in plasma cholesterol levels, but also because they have established benefits in reducing cardiovascular morbidity and mortality. These effects result primarily from a reduction in endogenous cholesterol biosynthesis and increased expression of low-density lipoprotein (LDL) receptors, thereby increasing the uptake and clearance of LDL-cholesterol from plasma. However, in the review by Andrea Poli, statins differ somewhat in their pharmacology and lipid-lowering effects. Although there have been few head-to-head trials among the statins, Paolo Rubba speculates on the basis of published literature that differences between statins could contribute to differences between agents in reducing cardiovascular events. On the other hand, it must be pointed out that cardiovascular disease risk reduction for all the statins is closely related to how much LDL lowering they produce.

Marcello Arca and Achille Gaspardone provide a succinct yet thorough review of the efficacy of atorvastatin in the primary and secondary prevention of cardiovascular events. Their discussion of primary prevention data focuses on results of the large ASCOT-LLA trial in hypertensive patients with plasma total cholesterol levels ≤6.5 mmol/L, which showed that treatment with atorvastatin for approximately 3 years significantly reduced the relative risk of primary coronary heart disease events compared with placebo. The beneficial effects of atorvastatin in patients with established cardiovascular disease have also been shown in various clinical settings. The authors review data from a number of secondary prevention trials with atorvastatin, including IDEAL, TNT, ALLIANCE and GREACE in patients with stable coronary heart disease (the latter two trials conducted in a 'real world' setting), MIRACL, PROVE-IT and IDEAL-ACS in patients with acute coronary syndrome, and AVERT, ARMYDA and ARMYDA-3 in patients undergoing invasive coronary interventions.

Marcello Arca's review of the efficacy of atorvastatin in the prevention of cardiovascular events in patients with diabetes and/or the metabolic syndrome highlights results from the primary prevention trial CARDS, in which atorvastatin significantly reduced the relative risk of cardiovascular events compared with placebo. Atorvastatin was also associated with a

similar reduction in the relative risk of cardiovascular events in the subgroup of hypertensive patients in the ASCOT-LLA trial who also had diabetes. Subgroup analyses of several secondary prevention trials with atorvastatin, including substudies of GREACE, TNT and PROVE-IT, also showed significant benefits in the prevention of cardiovascular events in patients with diabetes. However, results of a mixed primary and secondary prevention trial in patients with diabetes (ASPEN) did not show a reduction in major cardiovascular events with atorvastatin compared with placebo, despite a significantly greater reduction in LDL-cholesterol levels with the statin.

Although observational studies have not yet clearly defined an association between hypercholesterolaemia and stroke, the article by Achille Gaspardone and Marcello Arca, which reviews analyses of cerebrovascular prevention with atorvastatin and other statins from various primary (ALLHAT-LLT, ASCOT-LLA, CARDS, WOSCOPS) and secondary (4S, CARE, GREACE, HPS, LIPID, MIRACL, SPARCL, TNT) prevention trials, suggests that statins consistently reduce the risk of stroke; however, data are more robust for secondary prevention in patients with established coronary heart disease. In addition, results of the SPARCL study demonstrated significant benefits of atorvastatin versus placebo in the secondary prevention of cerebrovascular events in patients with a history of stroke or transient ischaemic attack (without coronary heart disease).

In the final article in the supplement, Marcello Arca provides an overview of safety and tolerability data for atorvastatin from postmarketing studies and meta-analyses which showed atorvastatin is generally well tolerated when administered at recommended therapeutic dosages. In addition, atorvastatin is associated with a relatively low incidence of muscular toxicity and is generally well tolerated in elderly patients.

Together, the articles in this supplement provide an excellent review of the pharmacology, clinical efficacy and tolerability profile of atorvastatin, highlighting key clinical trial data showing its benefits in the primary and secondary prevention of cardiovascular events.

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