Curated by Peter Lansberg, a Dutch lipidologist and educator, and reviewed by prof. Philip Barter, Past President of the International Atherosclerosis Society.

The IAS statin literature update will keep you up-to-date with all recent statin publications, using a curated approach to select relevant articles.

**Key publications**

**Elderly patients at risk for CVD – are statins of value**

The rationale for using high-dose, high-intensity statins in elderly patients is partly based on sub-analyses of the major randomized controlled CV outcome trials and large observational registries. Recently updated ESC guidelines included elderly patients (>75 years) in both the SCORE-OP (Older Patients) and therapeutic recommendations. IN this
retrospective observational study, based on data of a Californian Health Care organization, Patients > 75 years were more likely to suffer a cardiovascular complication compared to their younger patients (65-75 years). An HR: 1.42 (1.23-1.63) was noted for the very elderly patients. Moderate- or high-intensity statin prescriptions were observed significantly less in this cohort, OR:0.80 (0.74-0.86; P<0.001). Women, OR:0.85 (0.81-0.89) and underweight elderly, OR:0.45 (0.33-0.61), were less likely to be prescribed moderate or high-intensity statins as well. Efforts directed at exploring the reasons for these differences are warranted.


Comparing safety parameters between pitavastatin, atorvastatin and rosuvastatin users

Are Asians more susceptible to statins side effects than Caucasians, and are there clinically relevant differences between statins? These questions were addressed in a sub-analysis of the Taiwan National Health Insurance Research Database. Those that started treatment with atorvastatin, rosuvastatin, or pitavastatin and no diabetes were included. They were divided into three groups, 1. Pitavastatin 2-4 mg, 2. atorvastatin 10 and rosuvastatin 5-10 mg, and 3. Atorvastatin 20-40 mg and rosuvastatin 20 mg. The designated endpoint was a composite of hepatitis, myopathy, and new-onset diabetes (NODM). Patients were propensity score-matched based on age, sex, and year of recruitment. Each group consisted of 50 935 patients. The composite endpoint was observed 9.84% of the patients using pitavastatin and 10.88% plus 10.49% in the cohorts using low dosage and high dosage atorvastatin or rosuvastatin, respectively. The authors concluded that low dose statins, compared to pitavastatin, were associated with an increased risk for the composite endpoint (9.84% vs. 10.88%); HR: 1.12 (1.08-1.17). Noteworthy is that with the use of high-intensity statins, the risk of adverse events was higher (10.48%) compared to pitavastatin but lower compared to low dose statins, HR: 1.06 (1.02-1.10). No data were presented on LDL-c reductions in the three cohorts that would likely be less in the pitavastatin cohort than the high-dose statin users.


Review of the first in class Lp(a) lowering drugs, Pelacarsen

Statins remain the well-established first choice for reducing LDL-c. Despite the impressive success of high-dose, high-intensity statins to significantly reduce ASCVD risk, residual risk remains a formidable challenge in very-high-risk patients. This review provides
clinicians with up-to-date information on a new lipid-lowering drug and even a new class of drugs targeting elevated Lp(a). Pelacarsen is the new kid on the block that uses a unique antisense oligonucleotide approach to block the synthesis of apolipoprotein (a) and the formation of Lp(a). The phase I and II studies showed that a monthly dose of pelacarsen resulted in impressive reductions of Lp(a) of >50% and, depending on the dosage used, up to 80-90%. The safety profile of this new agent revealed no significant signals in terms of serious adverse events; injection site reactions were the most frequently reported complaints. A large phase III study is ongoing; the HORIZON study aims to evaluate MACE reductions in patients allocated to pelacarsen. In total, 7680 patients with established CVD and elevated Lp(a) (>70 mg/dl) will be included. The study is expected to be completed and published in 2024. Same in-class compounds are in the drug development pipeline.

Olpasiran (AMG860) has successfully completed a phase I study showing similar impressive efficacy and safety parameters that persisted over 6 months after a single dose. Olpasiran uses siRNA technology to suppress apo (a) synthesis.


**Switching to a polypill strategy for secondary prevention**

Despite recent well-established guidelines on both blood pressure management and lipid control, a large percentage of very high-risk patients are sub-optimally or even not treated. Strategies to simplify pharmacological regimens have successfully shown that a fixed-dose combination pill could be an attractive alternative compared to single pill strategies. In this review and expert opinion-based guideline, the CNIC polypill and algorithms providing guidance on the practical implementation of a polypill-based risk-reducing strategy are presented and explained. The CNIC polypill was developed by the Spanish Centre for Cardiovascular Research (CNIC), headed by prof. Valentin Fuster. The polypill contains three main ingredients, two in different dosages: ASA (100 mg), ramipril (1.5, 5, or 10 mg), and atorvastatin (20 or 40 mg). The algorithm was developed by an expert panel from Spain, Germany, Portugal, and Greece. The primary focus is secondary prevention patients grouped by ACS and chronic coronary syndromes, including stroke and peripheral artery disease. Using the polypill strategy would provide better guideline dictated LDL-c and blood pressure goal achievement for patients not on target. Combining the polypill with additional drugs to reach targets is integrated into the algorithm. Patients with well-controlled risk factors would be helped by a simplified treatment strategy to reduce their pill burden. The suggested approach is not a one-size-fits-all solution but does provide substantial improvement for both adherence and achieving guidelines-endorsed targets. Availability of the CNIC polypill in local pharmacies would be an essential hurdle to address before
Is atorvastatin the first-choice repurposed drug to improve COVID-19 outcomes

Innovative strategies to improve outcomes in COVID-19 patients that present with serious complications is expanding towards the repurposing of existing FDA approved drugs. Safe, effective, and affordable compounds that could change the course of the disease and reduce hospitalizations, ICU admission and death. A large transcriptomics database was queried for this study, and potential promising signals were combined with in vitro molecular docking analyses using lung organoid models. Over a 1000 FDA approved drugs were analysed and atorvastatin surfaced as one of the most promising candidates. Tests evaluated reduced transcriptional changes, effective binding to SARS-CoV-2 main protease and RNA-dependent polymerase as well as inhibiting viral entry into the organoid lung model. These fundamental studies are in congruence with small clinical trials as well as observational studies that showed protective effects of statins in general and specifically of atorvastatin to in COVID-19 patients admitted to hospital. The author’s findings support the currently ongoing larger clinical trials to support their findings. The technology they developed could be similarly applied when confronted with future pandemics.


Relevant publications


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