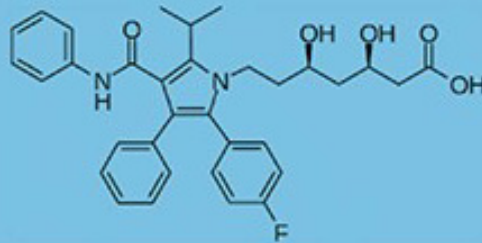


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**IAS STATIN**  
NEWSLETTER



INTERNATIONAL  
ATHEROSCLEROSIS  
SOCIETY

A CURATED WEEKLY UPDATE OF ALL STATIN PUBLICATIONS

Update - Week 03 & 04, 2022



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

### Different risk factors predict IS and ICH in CAD patients

Stable CAD patients are not only at risk for a recurrence but are also prone to develop ischemic or hemorrhagic strokes. This prospective follow-up study included 1428 Taiwanese stable CAD patients using standard medical therapy and were followed for a period of at least 4 years. Based on a multivariate logistic regression analysis, the risk for ischemic stroke was associated with baseline serum levels of myeloperoxidase (MPO), HR:1.89 (1.16-3.10, p=0.01), and statin use, HR:0.37 (0.17-0.79; P=0.01). In contrast with risk for hemorrhagic stroke, which was associated with age, HR:1.07 (1.00-1.14; P=0.04) and ARB use, HR: 0.37 (0.17-0.79; P=0.01). these findings point to possible different mechanisms for developing an ischemic or hemorrhagic stroke and warrant potential different therapeutic approaches to reduce the risk for these cerebral vascular events. Prognostic indicators for the onset of ischaemic versus haemorrhagic stroke in stable coronary artery disease.

Medicine (Baltimore) 2021; 100:e27973. <http://www.ncbi.nlm.nih.gov/pubmed/?term=35049202>

### Reduced their CVD risk in NASH patients using a polypill

NASH is associated with an increased CVD risk, and controlling CV risk factors is relevant in these patients. This randomized prospective 5-year follow-up study included 2400 NASH patients. NASH was diagnosed using ultrasound and elevated liver enzymes. In the final analysis, 787 patients used the polypill, and 721 were in the control group. The trial

endpoints were major CV events (fatal myocardial infarction, sudden death, new-onset heart failure, coronary artery revascularization procedures, fatal and non-fatal stroke, or hospitalization for an acute coronary event); the secondary outcomes were changes in liver function parameters, blood pressure, lipid profiles, and BMI adjusted. MACE risk was 0.35 (0.17-0.73) for participants that used the polypill vs. 0.73 (0.49-1.0) in the control group. Although numerical de events observed were halved inpatient using the polypill, this difference was not statistically significant. The median adherence in the polypill group was 80.4%. High adherence (>70% of provided polypills) was associated with a significantly decreased MACE risk, RR:0.46 (0.30-0.71) when compared to controls and compared to the low adherence group, RR:0.53 (0.33-0.86). For the secondary endpoints of liver function tests participants those with NASH and using the polypill, there was a significant decrease after 60 months of follow-up in patients taking the polypill, an intragroup difference of -12.0 IU/L (-14.2 to -9.6). This is the first report on the use of polypill in patients with NASH/NAFLD. The benefits observed in the PolyIrran-Liver trial look encouraging and warrant further properly designed randomized trials to confirm these promising findings. Merat S, Jafari E, Radmard AR *et al.* Polypill for prevention of cardiovascular diseases with focus on non-alcoholic steatohepatitis: the PolyIrran-Liver trial. *Eur Heart J* 2022.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=35048107>

### Patients diagnosed with hypertension should use a statin – HOPE-3 trial

revention patients with an annual ASCVD risk of approximately 1% + stage I hypertension. No benefits were observed in patients that used candesartan/HCT + placebo. But patients that used rosuvastatin + placebo or rosuvastatin + candesartan/HCT noted a significant ASCVD risk reduction; HR:0.75 (0.64-0.88; P<0.01) and HR:0.72 (.57-0.89; P<0.003) respectively. The greatest benefits were observed in the patients with the highest tertile of systolic blood pressure. The authors review the available trial data on hypertension control and, combined with the HOPE-3 study data, suggest a standard statin therapy for patients diagnosed with stage II hypertension (systolic blood pressure > 140 mm Hg or diastolic blood pressure > 90 mm Hg) to further reduce their long term ASCVD risk.

McNavish DE, German CA, Shapiro MD. Should a Statin be Given to All Hypertensive Patients? *Curr Hypertens Rep* 2022; 24:21-27. <http://www.ncbi.nlm.nih.gov/pubmed/?term=35072922>

### End stage renal disease patients and statins, the debate continues

Statins failed to show benefit in patients with advanced renal disease on dialysis. The 4D and AURORA trials, using atorvastatin and rosuvastatin, respectively, were both unsuccessful. Despite these findings, the use of statins in patients with advanced renal disease remains under debate. In this PCI registry, 201 chronic hemodialysis patients who had a first PCI were followed for a median period of 2.8 years (0-15.2 years). Patients were divided into 2 groups; with or without statins and with or without high LDL-c (93 mg/dL was used as cut-off). The primary endpoint was CV death, and secondary endpoints included all-cause mortality, non-cardiovascular death, and a 3-point MACE (CV-death, non-fatal myocardial infarction, and stroke). Both Kaplan Meier and multivariate Cox proportional hazard analysis were used to determine the efficacy of statins in this special patient population. Both endpoints were significantly reduced in statin-treated patients. No differences were noted based on median LDL-c levels at time of PCI (P=0.11) Statins were independent predictors for reduced risk of CV death, HR: 0.43 ((0.18-0.88; P=0.02); all-cause death, HR:0.50 (0.29-0.84; P=0.007) and 3P-MmACE, HR:0.50 (0.25-0.93, P=0.03). Despite the limitations associated with the study design, statins used showed promising results in end-stage renal disease patients that had a PCI, intriguingly the observed benefits seemed to be

unrelated to the LDL-c lowering properties of statins. Patients that used statins were less likely to experience CVD complications.

Wang WT, Wu TC, Tseng WK *et al*

Funamizu T, Iwata H, Chikata Y *et al*. A Prognostic Merit of Statins in Patients with Chronic Hemodialysis after Percutaneous Coronary Intervention-A 10-Year Follow-Up Study. Journal of clinical medicine 2022; 11. <http://www.ncbi.nlm.nih.gov/pubmed/?term=35054080>

## Statins and ACEi a dynamic duo

Atherosclerosis starts, progresses, and eventually terminates in (fatal) complications due to endothelial dysfunction. Depending on their severity and duration, CV risk factors interact with endothelial cells to propagate the atherosclerosis process. Two of the most prominent risk factors, hypertension, and dyslipidemia, interact and synergistically accelerate vascular wall pathological changes. Reciprocally managing both risk factors simultaneously will result in greater benefits than simply adding up their individual effects. Both ACEi and statins have shown that their well-recognized CVD benefits reach beyond blood pressure and cholesterol reduction. Both Ang II and NO, critical players in endothelial function, affect oxidative stress, inflammation, and coagulation; both drug classes possess pleiotropic properties that target Ang II and NO and protect the endothelium. This review provides an in-depth overview of the clinical evidence that supports the synergistic benefits of these two drug classes. Statins reduce AT1 receptor expression as well as cholesterol accumulation in macrophages. Both statins and ACEi reduce LDL oxidation, inflammation, matrix degradation in the fibrous cap, smooth muscle cell proliferation/migration, and endothelial dysfunction. An ASCVD fighting duo that is commonly available for an affordable price globally should be part of treatment protocols for most patients with CVD or at risk for ASCVD complications.

Borghi C, Levy BI. Synergistic actions between angiotensin-converting enzyme inhibitors and statins in atherosclerosis. Nutrition, metabolism, and cardiovascular diseases : NMCD 2021. <http://www.ncbi.nlm.nih.gov/pubmed/?term=35082055>

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## Relevant publications

1. Galarza-Delgado DA, Colunga-Pedraza IJ, Azpiri-Lopez JR *et al*. Statin indication according to the 2019 World Health Organization cardiovascular disease risk charts and carotid ultrasound in Mexican mestizo rheumatoid arthritis patients. Adv Rheumatol 2022; 62:4. <http://www.ncbi.nlm.nih.gov/pubmed/?term=35078534>
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14. Naghavi M, Kleis S, Tanaka H *et al*. High Frequency of Microvascular Dysfunction in US Outpatient Clinics: A Sign of High Residual Risk? Data from 7,105 Patients. Int J Vasc Med 2022; 2022:4224975. <http://www.ncbi.nlm.nih.gov/pubmed/?term=35036009>
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