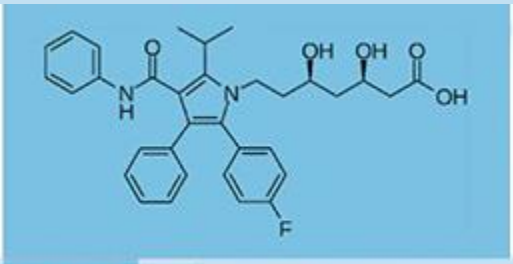
IAS STATIN NEWSLETTER



INTERNATIONAL ATHEROSCLEROSIS SOCIETY

A CURATED WEEKLY UPDATE OF ALL STATIN PUBLICATIONS

Update - Week 17, 2021

**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

Are statins safe in CKD patients

Patients with chronic kidney disease (CKD) have an increased CVD risk. Statins are often prescribed in these patients; however, conflicting evidence regarding harms vs. benefits can be confusing. This meta-analysis re-evaluated all relevant peer-reviewed published studies to support clinicians deciding which CKD patients should be treated with statins and dosage. Included in this analysis were 33 randomized controlled clinical trials that included 37 391 CKD patients. In summary, urine albumin excretion was significantly reduced in statin allocated patients vs. controls, weighted mean differences (WMD) -2.04 (-353 to -0.56; P=0.007). A similar response was observed for protein excretion, WMD: -0.58 (-0.95 to -0.21; P=0.002). Creatinine clearance increased, WMD 0.86 (0.32 to -1.41; P=0.002). Glomerular filtration rate and serum creatinine were not significantly different between the two groups. The authors concluded that statin use in CKD patients was associated with lower urinary albumin and protein excretion and increased creatinine clearance. Atorvastatin, pravastatin, and pitavastatin were their statins of choice in CKD patients. Large-scale trials are warranted to improve our understanding of the effects of statins in

renal patients.
Efficacy of statins on renal function in patients with chronic kidney disease: a systematic review and meta-analysis. Ren Fail 2021; 43:718-728Zhao L, Li S, Gao Y. http://www.ncbi.nlm.nih.gov/pubmed/?term=33926359

Statins potential benefits in COVID-19 patients explored

What is the rationale for prescribing LDL-c lowering statins for patients suffering from a SARS-CoV-2 viral infection? The authors of this review summarise the basic concepts and potential therapeutic benefits of statins in COVID-19 patients. Lipid metabolism plays a pivotal role in viral infections, supports their life cycle, and weakens the host's defenses. Viruses can hijack and alter the expression of genes that regulate the mevalonate pathway to improve their chances of replication. Statins have been shown to reduce cholesterol concentrations of plasma membranes in cells, used as viral entry points, resulting in reduced viral plasma concentrations and failure to internalize viruses. Statins are associated with immunomodulatory-, anti-inflammatory-, and anti-thrombotic effects. They can Improve endothelial function and blunt inflammation in the vascular wall of arterial vessels and capillaries. These are pleiotropic effects that statins seem to possess. The benefits and potential harms of statins in COVId-19 patients are highlighted in this review. The authors provide a historical context and an update of our current understanding and evidence on how statins could help prevent serious, life-threatening SARS-CoV-2 complications.
Lipid homeostasis and mevalonate pathway in COVID-19: Basic concepts and potential therapeutic targets. Progress in lipid research 2021; 82:101099Proto MC, Fiore D, Piscopo C *et al.* http://www.ncbi.nlm.nih.gov/pubmed/?term=33915202

Dose escalation in CHD patients using high intensity high dose statin

Dose escalation is a significant hurdle for patients and physicians. Is it safe and what to expect from increasing the statin dose or adding ezetimibe when a patient already uses high intensity, high dose statin. In this retrospective analysis of a single institute, 1159 Korean CVD patients achieved an LDL-c of 55-99 mg/dL using atorvastatin 40 mg, or an equivalent regimen (rosuvastatin 20 mg or simvastatin 10 mg + ezetimibe 10 mg) were included. The 164 patients with LLT dose escalation were propensity score-matched (1:2) to 328 controls without dose escalation. The primary outcomes: major adverse cardiovascular and cerebrovascular events (MACCE) and all-cause death. At a median follow-up period of 1.93 years, dose escalation was associated with a reduction in MACCE, 1.72 vs. 3.38/100 person-years; HR: 0.34 (0.14-0.83; p=0.018). A similar trend, albeit not statistically significant, was noted for mortality, 0.86 vs.1.02; HR:0.58 (0.15-2.19; p=0.42). There was no difference in

outcomes between the MACCE components. Kaplan-Meier survival curves showed a lower risk of MACCE in patients with dose escalation; HR:0.36 (0.12-0.96; p=0.040), Mortality exhibited a reduced trend, but this was not statistically significant; HR:0.30 (0.04-2.48; p=0.26). Based on these observational, findings the authors concluded that dose escalation in Korean patients using a high dose high-intensity statin was associated with improved MACCE outcomes supports using more aggressive LLT this population.
Escalation of liPid-lOwering therapy in patientS wiTh vascular disease receiving HIGH-intensity statins: the retrospective POST-HIGH study. Scientific reports 2021; 11:8884Ha J, Lee B, Park JM *et al.* http://www.ncbi.nlm.nih.gov/pubmed/?term=33903685

Statin effects on neuro-cardiac stress response in primary prevention population

The anti-inflammatory effects of statins are further reaching with unexpected benefits in the central nervous system (CNS). Stress contributes to adverse CVD outcomes, and prolonged exposure to inflammation is associated with harmful neuro-cardiac effects. In this retrospective study, the anti-inflammatory and neuroprotective effects of statins were evaluated in 267 patients that had echocardiography and an 18F-fluorodeoxyglucose (18F-FDG) positron emission tomography (PET). The latter allowed for measuring the brain's amygdala activity as well as vertebral bone marrow metabolism. Neural stress responses were associated with increased inflammatory activity in the bone marrow (r = 0.152, p = 0.015) and a subclinical reduction in left ventricular ejection fraction (LVEF, r = -0.138, p = 0.025). Based on a fully adjusted linear regression model, statin treatment was an independent, negative predictor of amygdalar metabolic activity (B-coefficient -0.171,p = 0.043). These hypothesis generation findings point towards a potential link between the anti-inflammatory properties of statins and a reduction in the neural stress response that could improve cardiovascular outcomes. The authors concluded that these intriguing neuro-hematopoietic-vascular axis findings might help explore new primary and secondary CVD prevention concepts and warrant larger prospective studies to explore these initial observations.
Potential Impact of Statins on Neuronal Stress Responses in Patients at Risk for Cardiovascular Disease. Journal of personalized medicine 2021; 11Diggelmann F, Bengs S, Haider A *et al.* http://www.ncbi.nlm.nih.gov/pubmed/?term=33916056

Managing statin intolerance, a practical guidance

In this concise and practice-oriented review, the authors discuss both the mechanisms of muscle-related side effects and how to improve adherence or provide alternatives to patients confronted with statin tolerability issues. The pathophysiology of statin-associated muscle symptoms (SAMS) is not fully elucidated, but drug-drug interactions and direct

effects of statins on mitochondrial function are seen as essential contributors. Practical considerations such as vitamin D deficiency as well as statin-based changes in treatments are suggested. Lowering the dosage, changing the statin, and/or adding non-statin LDL-c lowering drugs such as ezetimibe, bile acid sequestrants, PCSK9ab, and the recently introduced bempedoic acid are discussed. Alternative nutraceutical therapies such as red yeast rice, plant sterols, berberine, curcumin, polydatin, quercetin, and fish oils are potential complementary suggestions. Future LDL-c lowering therapies, such as Inclisiran (PSCK9siR), ANGPTL3 antibodies and CRISPR-Cas9 gene editing, are mentioned as well. Statin intolerance: new data and further options for treatment. Current opinion in cardiology 2021; Diaconu CC, Iorga RA, Furtunescu F *et al.*
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Relevant publications

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http://www.ncbi.nlm.nih.gov/pubmed/?term=33909607
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http://www.ncbi.nlm.nih.gov/pubmed/?term=33916281
3. COVID-19: Direct and Indirect Mechanisms of Statins. Int J Mol Sci 2021; 22Pawlos A, Niedzielski M, Gorzelak-Pabiś P *et al.*
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http://www.ncbi.nlm.nih.gov/pubmed/?term=33903311
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12. **Adoption of PCSK9 Inhibitors Among Patients With Atherosclerotic Disease. J Am Heart Assoc 2021; 10:e019331Dayoub EJ, Eberly LA, Nathan AS *et al.*** http://www.ncbi.nlm.nih.gov/pubmed/?term=33904340
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