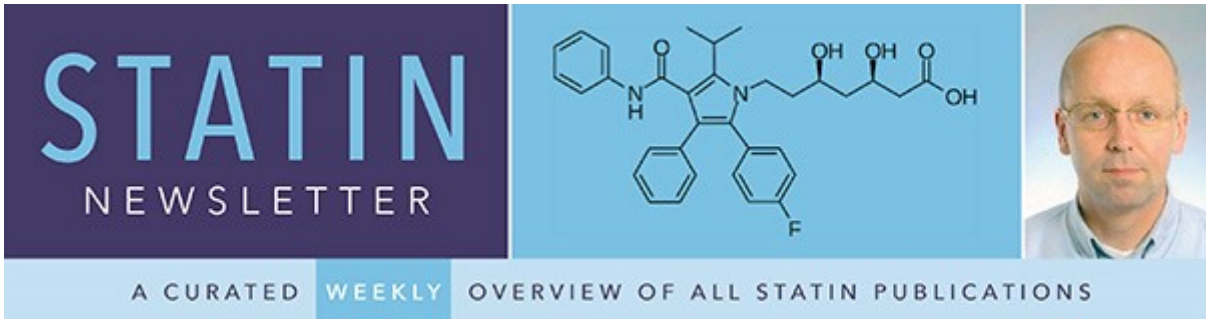

Update week 47 & 48 - 2022

Dr. Peter Lansberg is a Dutch lipidologist, educator and innovator. He has been instrumental in setting up The Dutch National Lipid Clinic Network, the Dutch Lipid Clinic Criteria for Familial Hypercholesterolemia (FH), and the Dutch National FH screening program

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The Statin Newsletter will keep you up-to-date with all recent statin publications. Based on a curated approach to select relevant articles.

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Key Publications

1. **Atorvastatin tops list for muscle tollerance**
2. **SAMS and chronic pain disorders**
3. **Vitamin D fails to improve SAMS**
4. **Atorvastain and Cancer, from foe to frien**
5. **Delays in reaching LDL-c targets costs money and life's**

Muscle tolerability of Atorvastatin superior compared to simvastatin and pravastatin

A network meta-analysis of 83 randomized controlled trials and 170,148 patients was conducted to compare the muscle safety of individual statins. The results showed that statins as a class were only slightly associated with an increase in muscle symptoms compared to control, with no significant difference found between individual statins in the incidence of muscle symptoms, myalgia, myopathy, rhabdomyolysis, creatine kinase (CK) levels, or discontinuation due to muscle adverse events. In the dose-level network meta-analyses, only moderate atorvastatin was found to have a lower risk of CK levels compared to moderate simvastatin and moderate pravastatin. Lipophilic statins and those metabolized by the liver cytochrome P450 3A4 were not associated with an increased risk of muscle adverse events. The results are consistent with previous meta-analyses and suggest that statins are generally safe for muscle, and moderate atorvastatin may be superior to equivalent doses of simvastatin and pravastatin in muscle tolerability.

Hou Q, Chen Y, Zhang Y, Pang C. **Comparative Muscle Tolerability of Different Types and Intensities of Statins: A Network Meta-Analysis of Double-Blind Randomized Controlled Trials.** Cardiovasc Drugs Ther 2022. http://www.ncbi.nlm.nih.gov/pubmed/?term=36447018

Patients with statin related myalgia, more likely to suffer from chronic pain disorders

The study aimed to compare the occurrence of chronic pain among patients on statin therapy who developed myalgia with those who did not. 112 statin-treated patients were included, 56 with a diagnosis of statin-associated muscle symptoms (SAMS) and 56 without. The study used verified questionnaires to assess fibromyalgia, pain intensity, functional impairment, anxiety, and depression in the study population. Results showed that patients with statin myalgia were more likely to fulfill the diagnostic criteria for fibromyalgia compared to those without (19.6% vs. 0). Patients in the SAMS group exhibited higher levels of anxiety and depression compared to the control group. Female sex, higher scores on the Brief Pain Inventory pain intensity scale, and a Hamilton rating scale level indicative of an anxiety disorder were significant predictors for fibromyalgia in patients presenting with statin myalgia. The study highlights the significant percentage of patients diagnosed with statin myalgia who have concomitant fibromyalgia, depression, or anxiety disorder. Detection of these patients and treatment of their primary pain disorders or psychiatric illnesses has the potential to prevent unnecessary cessation of effective statin therapy.
Sheinin R, Nogueira AR, Bragazzi NL *et al.* Are Chronic Pain Syndromes the Reason for Statin-associated Muscle Symptoms? The Israel Medical Association journal : IMAJ 2022; 24:719-726. http://www.ncbi.nlm.nih.gov/pubmed/?term=36436038

Vitamin D shows now benefit in preventing SAMS

The VITAL trial aimed to test whether vitamin D supplementation was associated with the prevention of statin-associated muscle symptoms (SAMS) and a reduction in statin discontinuation. Participants were enrolled in a randomized, placebo-controlled, double-blind clinical trial of vitamin D supplementation. Statins were initiated by 1033 participants assigned to vitamin D and 1050 participants assigned to placebo. The results showed that SAMS were reported by 317 participants assigned to vitamin D and 325 assigned to placebo with an adjusted odds ratio of 0.97. Statins were discontinued by 137 participants assigned to vitamin D and 133 assigned to placebo with an adjusted odds ratio of 1.04. The results were consistent across pretreatment 25-hydroxy vitamin D levels. The study found that vitamin D supplementation did not prevent SAMS or reduce statin discontinuation, and a clinically important treatment effect from vitamin D on SAMS is unlikely.
Hlatky MA, Gonzalez PE, Manson JE *et al.* Statin-Associated Muscle Symptoms Among New Statin Users Randomly Assigned to Vitamin D or Placebo. JAMA cardiology 2023; 8:74-80. http://www.ncbi.nlm.nih.gov/pubmed/?term=36416841

Atorvastatin as adjuvant in cancer therapy – A comprehensive review

Cancer is a challenging disease to manage and various treatments are available, including chemotherapy, targeted therapy, radiotherapy, and immunotherapy. Some agents are being investigated as adjuvants to improve the effectiveness of cancer treatments. Statins, which are known for reducing lipids, have shown potential as a cancer treatment. Atorvastatin, a HMG-CoA reductase inhibitor, has been shown to affect the proliferation, migration, and survival of cancer cells. Numerous studies have been conducted to understand the antitumor effects of atorvastatin. Different types of cancer have been evaluated and the findings suggest that atorvastatin has the highest antitumor effect compared to other statins. Atorvastatin has also been shown to improve the efficacy of chemotherapy and radiotherapy. Additionally, it has been shown to have antioxidant, anti-inflammatory, and immunomodulatory properties, which help to inhibit oxidative stress damage to biological systems. However, more research is needed to fully understand the mechanisms by which atorvastatin affects cancer cells.
Shaghaghi Z, Alvandi M, Farzipour S *et al.* A review of effects of atorvastatin in cancer therapy. Medical oncology (Northwood, London, England) 2022; 40:27. http://www.ncbi.nlm.nih.gov/pubmed/?term=36459301

Delay in reaching LDL-c goals has a price

This study aimed to quantify the health economic impact of delayed lipid-lowering intensification for statin-treated patients who have not reached low-density lipoprotein

cholesterol (LDL-C) therapeutic goals. Using a lifetime Markov cohort model, the study compared the impact of intensifying lipid-lowering treatment with high-intensity statins or statins and ezetimibe to standard of care in 1000 patients with uncontrolled LDL-C and moderate to high risk of coronary heart disease (CHD). The results showed that achieving LDL-C control with no delay with high-intensity statins prevented 29 CHD events and resulted in 30 extra quality-adjusted life years, with an incremental cost-effectiveness ratio of AU$13 205/quality-adjusted life year, versus 22 CHD events and 16 quality-adjusted life years with a 5-year delay. The study also showed that ezetimibe prevented 53 CHD events and resulted in 45 extra quality-adjusted life years with no delay, and 40 CHD events and 29 quality-adjusted life years with a 5-year delay. The study concluded that delaying attainment of LDL-C goals leads to lost therapeutic benefit and a waste of resources, and that urgent policies are needed to improve LDL-C goal attainment in statin-treated patients.
Marquina C, Morton J, Zomer E *et al.* **Lost Therapeutic Benefit of Delayed Low-Density Lipoprotein Cholesterol Control in Statin-Treated Patients and Cost-Effectiveness Analysis of Lipid-Lowering Intensification.** Value in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research 2022. http://www.ncbi.nlm.nih.gov/pubmed/?term=36442832

Relevant Publications

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2. Lin CP, Hsiao FC, Wu CT *et al.* Beneficial Effects of Fixed-Dose Combination of Amlodipine and Atorvastatin in Patients with Concomitant Hypertension and Hypercholesterolemia: A Multi-Institutional Cohort Study. Acta Cardiologica Sinica 2022; 38:736-750. http://www.ncbi.nlm.nih.gov/pubmed/?term=36440238
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