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

Statin for VTE prophylaxis in patients with endometrial cancer

The repurposing of existing drugs for indications beyond their primary target is an attractive and plausible strategy. Endometrial cancer (EC) is associated with an increased VTE risk. Although this type of cancer prognosis is favorable, addressing the frequently reported comorbidities, including VTE, can improve long-term outcomes. In this review, both aspirin and statins are evaluated for their efficacy to prevent VTE’s. Studies that assessed the effects of both drugs on VTE in women with EC are presented, seven statins studies plus four aspirin trials and one meta-analysis. Metabolic pathways of thrombosis and the specific inhibitory properties of aspirin and statins are explained. The authors suggest that aspirin
use was associated with a modest benefit on VTE prophylaxis and improved survival in obese older women (<60 years) that presented with type I cancer. Statin use was associated with enhanced survival and reduced VTE risk in women with type II endometrial cancer. The combination of statin + aspirin would be the preferred choice for obese women with type II cancer.


**Combining a statin with ezetimibe, what to expect?**

The combination of statin + ezetimibe is an effective combination therapy for lowering LDL-c. Similar strategies that have been widely accepted for blood pressure control are now embraced by recent European and US lipid management guidelines—comparing the safety and LDL-c lowering efficacy of rosuvastatin (R) 2.5 mg, 5 mg monotherapy, and ezetimibe (E) 10 mg vs. rosuvastatin 2.5 mg + ezetimibe 10 mg, in Korean hypercholesterolemic patients. This was a multi-center randomized controlled 8-week study in 297 patients. The combination of R (2.5 mg) + E (10 mg) showed superior LDL-c reductions of ~45.7% (~18.6%) vs ~16.7% (~14.7%, p < 0.0001) in the E 10 group, ~32.6% (~15.1%, p < 0.0001) in the R 2.5 group, and ~38.9% (~13.9%, p = 0.0003) in the R 5 group. All patients in the R 2.5 + E 10 group reached guideline dictated LDL-c targets, vs. 13% in the E 10 group, 46.5% in the R 2.5 group, and 65.2% in the R 5 group. Adverse events were reported by 7 (2.5%) of the participants. Discontinuation occurred in one patient in the R+E group and one patient in the R 2.5 group. A combination of low-dose rosuvastatin with ezetimibe was associated with superior LDL-c reductions compared to monotherapy with R 2.5, 5, or E 10. Lee SA, Kim W, Hong TJ et al. Effects of Fixed-Dose Combination of Low-Intensity Rosuvastatin and Ezetimibe Versus Moderate-Intensity Rosuvastatin Monotherapy on Lipid Profiles in Patients With Hypercholesterolemia: A Randomized, Double-Blind, Multicenter, Phase III Study. Clinical therapeutics 2021. [http://www.ncbi.nlm.nih.gov/pubmed/?term=34429197](http://www.ncbi.nlm.nih.gov/pubmed/?term=34429197)

**Can statins improve survival in newly initiated dialysis patients?**

This sub-analysis of the South Korean nationwide claims database evaluated the benefits of starting statins therapy in newly initiated dialysis patients. This was a retrospective observational propensity score-matched cohort study of 1 596 patients who started dialysis between 2010 and 2017 and initiated statins within the first year of dialysis. Propensity score matching was based on the following criteria: age, sex, time of dialysis initiation, and underlying diabetes mellitus and hypertension. Primary endpoints were all-cause mortality and major cardiovascular events (MACE). The total number of follow-up years was 9438; during this follow-up, 468 patients died, and 264 MACE occurred. Statin use was associated

Should cardiotoxic chemotherapy be combined with statins to preserve LVEF

A new specialization, cardio-oncology, provides expert care for the molecular and clinical alterations in the cardiovascular system during the different methods of treatment of cancer, especially chemotherapy and targeted therapy. In this review, the authors explored the potential benefits of statins on left ventricular ejection fraction and cardiomyopathy in patients treated with cardiotoxic chemotherapy. For this meta-analysis, seven studies with 3042 patients were included; 1382 used concomitant statins with their chemotherapy regimen; 1660 control patients used chemotherapy only. Statin use was associated with improved cardiac outcomes. Patients in the control group had a more significant decline in LVEF (-6.08% [-8.55—3.61. P<0.001). The incidence of cardiomyopathy was significantly lower in the statins users, OR:0.41 (0.28-0.60. P<0.001). The findings of this meta-analysis provide support for the cardioprotective effects of statins in cancer patients treated with cardiotoxic chemotherapeutic agents. Additional large-scale RCTs are warranted to corroborate these findings.


REDUCE-IT and STRENGTH a conundrum explained

Recently, two large placebo-controlled randomized trials using omega-3 fatty acids plus statins in high-risk, hypertriglyceridemic individuals showed contrasting and confusing results. The REDUCE-IT study compared eicosapentaenoic acid (EPA) with a mineral oil-based placebo, and in the STRENGTH study, a combination of EPA and EPA + docosahexaenoic acid (DHA) vs. a corn oil-based placebo. The REDUCE-IT study showed an
impressive 25% reduction in major cardiovascular events; the STRENGTH trial was terminated prematurely due to futility. The debates on these contrasting outcomes focus on the different types of fish oils to explain the superior benefits of EPA vs. no effect of EPA + DHA. An alternative explanation suggests that mineral oil is not an inert placebo and negatively affects LDL-c and ASCVD risk. The benefits of the EPA result from an increase of ASCVD risk in the “placebo” group that used mineral oil. The authors of this study used patient data collected in the Copenhagen General Population Study (CGPS). Patients were selected based on the inclusion criteria of both studies. Follow-up periods (4.9 years in REDUCE-IT and 3.5 years in STRENGTH) were extrapolated as well. Biomarkers at baseline and study completion (LDL-c, triglycerides, and hs CRP) were also mirrored. When comparing the outcomes for both studies in the CGPS, a risk reduction, HR of 0.88 (0.84-0.93) in the CGPS mimicking the REDUCE-IT study and an HR of 0.96 (0.93-0.99) was observed for CGPS participants simulating the STRENGTH study. This contrasts with the reported results of HR: 0.75 (0.68-0.83) in the REDUCE-IT and HR: 0.99 (0.90-1.09) in the STRENGTH studies. The authors concluded that the contrasting outcomes in the two studies could be partly explained by a difference in the oils used in the placebo group, but not the active fish oils triggered changes on hsCRP, LDL-c, and triglycerides. The observed 13% risk reduction is likely the result of other effects of EPA or mineral oil. Doi T, Langsted A, Nordestgaard BG. A possible explanation for the contrasting results of REDUCE-IT vs. STRENGTH: cohort study mimicking trial designs. Eur Heart J 2021. http://www.ncbi.nlm.nih.gov/pubmed/?term=34455435

Relevant publications


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**Basic Science publications**


10. Ibrahim SSA, Kandil LS, Ragab GM, El-Sayyad SM. Micro RNAs 26b, 20a inversely correlate with GSK-3β/NF-κB/NLRP-3 pathway to highlight the additive promising effects of atorvastatin and quercetin in experimental induced arthritis. Int Immunopharmacol 2021; 99:108042.


14. Erratum to chemoprotective effect of atorvastatin against benzo(a)pyrene-induced lung cancer via the inhibition of oxidative stress and inflammatory parameters.