



Management Strategies for Statin Intolerance

Statin therapy remains the most effective LDL-lowering intervention and is highly efficacious in both primary and secondary prevention of clinical ASCVD. Although generally well-tolerated, associated side effects can be seen – myalgias being the most common reason for patients to discontinue therapy.

The **American College of Cardiology Statin Intolerance App** provides clinicians with a systematic approach in the management and treatment of patients reported to have experienced muscle-related symptoms while on a statin. Key benefits of the app include:

- Thorough evaluation and management of potential intolerance
- Generates clinician-patient conversation
- Provides questions to assess symptoms
- Drug interactions and comparison of statin characteristics

Approaches to manage muscle-related symptoms attributed to statins:

- Alternative statin based upon pharmacologic profile:
 - Hydrophilic statins (rosuvastatin, pravastatin) have been shown to have less severe myalgias (lipophilic statins are commonly associated with myalgias, with simvastatin having the greatest lipophilicity)
- Re-challenge with the same statin but at a lower dose:
 - Intermittent dosing with long half-life statins (atorvastatin, rosuvastatin) can result in a ~20-40% reduction in LDL-C levels (although no cardiovascular [CV] outcomes studies have been established to identify the CV benefit of this specific approach)
- Non-statin agents as monotherapy or additions to a maximally tolerated statin dose should be considered next:
 - Ezetimibe: ~15-25% LDL-C reduction
 - IMPROVE-IT trial demonstrated reduction in CV events but did not reduce death
 - Bempedoic acid: ~15-20% LDL-C reduction as monotherapy vs. ~25-30% in combination with ezetimibe
 - Ongoing CLEAR Outcomes trial is studying patients who are statin intolerant and at high risk for CV disease given treatment with bempedoic acid vs. placebo
 - PCSK9 inhibitors: ~45-60% LDL-C reduction
 - FOURIER trial studied patients at high risk of CV disease given treatment with evolocumab to have reduced CV events, but did not reduce death

Other important modifications include:

- Lifestyle changes (diet, exercise, smoking cessation) play an important role in further reduction of cholesterol levels and CV risk factors
- Vitamin D deficiency (levels ≤ 32 ng/mL) and reduced production of coenzyme Q (CoQ10) are thought to be associated with muscle dysfunction and pain
 - Supplementation of vitamin D or CoQ10 can provide replenishment of stores without significant side effects and be safely used in statin-intolerant patients.