Baptist Health
HEART INSTITUTE

How to Handle Statin Intolerance in the High Risk Patient

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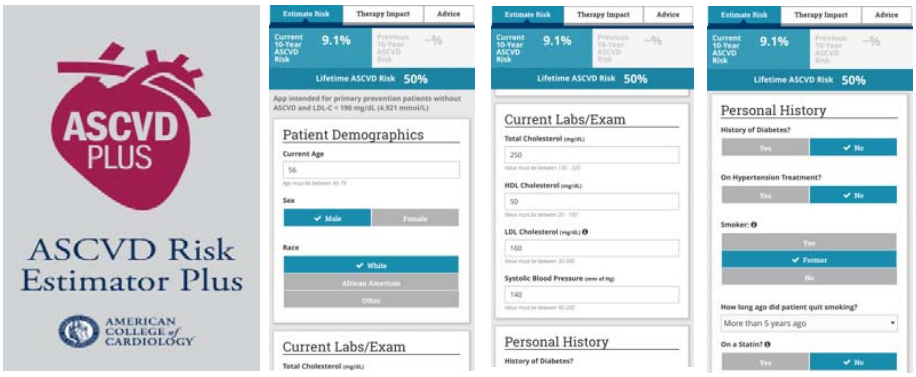
Disclosures: None

Definition of "High Risk"

- Primary Prevention
  - ASCVD Risk Calculator
  - Adults >21 yrs, LDL ≥ 190 mg/dl
  - Adults 40-75, + Diabetes, no ASCVD, LDL 70-189
  - Adults 40-75, no Diabetes/ASCVD, LDL 70-189 and 10 yr estimated ASCVD risk ≥ 7.5%
- Secondary Prevention
  - All patients with "vascular disease"
    - MI, Stable angina, Unstable angina, coronary or other arterial revascularization, stroke, TIA or PAD

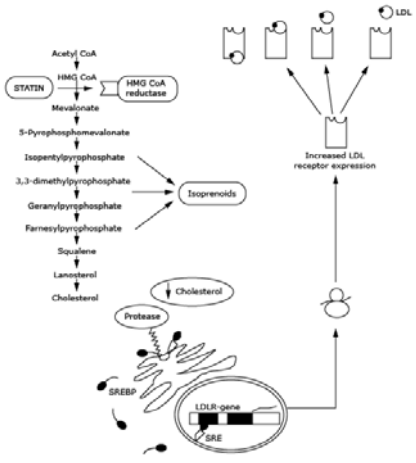


Lipid monotherapy proven to lower the risk of Stroke, MI and Death

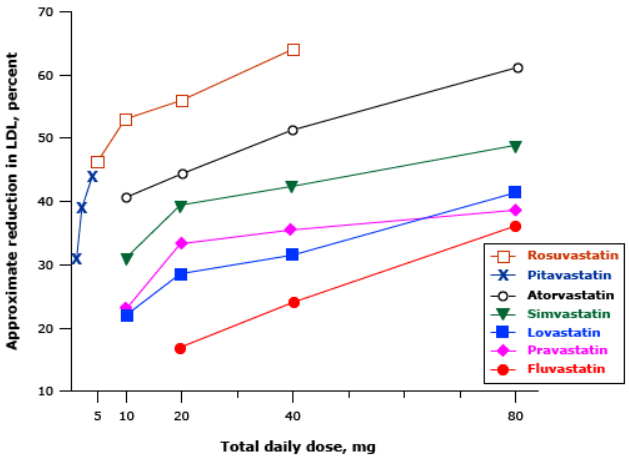
Statins

PCSK9 Inhibitors

Statins MOA



Statin Comparison



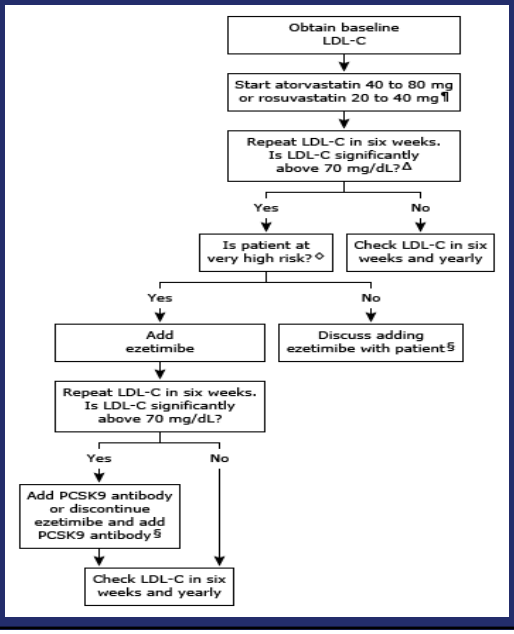
Intensity of Rx

High-Intensity Statin Therapy	**Moderate-Intensity Statin Therapy**	**Low-Intensity Statin Therapy**
Daily dose lowers LDL-C, on average, by approximately ≥50%.	Daily dose lowers LDL-C, on average, by approximately 30%–<50%.	Daily dose lowers LDL-C, on average, by <30%.
Atorvastatin 40–80 mg **Rosuvastatin 20–40 mg**	**Atorvastatin 10–20 mg** **Fluvastatin 40 mg twice daily** Fluvastatin XL 80 mg **Lovastatin 40 mg** Pitavastatin 2–4 mg **Pravastatin 40–80 mg** **Rosuvastatin 5–10 mg** **Simvastatin 20–40 mg**	Fluvastatin 20–40 mg **Lovastatin 20 mg** Pitavastatin 1 mg Pravastatin 10–20 mg Simvastatin 10 mg

Secondary Prevention with Statins

- Patients with ASCVD are at HIGH risk for CV events (Stroke, MI and CV death).
- Statins reduce CV events and All-cause mortality.
  - For every 40 mg/dl reduction in LDL
    - MACE reduced by 20-25%
    - All-Cause mortality reduced by 10%
- Except PCSK9 inhibitors, no other agents have been proven to prevent CVA/MI/Death as monotherapy.
  - Niacin, Fenofibrates , Bile Acid Sequestrants
  - Ezetimibe as Add-On therapy to statins slightly lowers Combined Endpoint of CV death, nonfatal MI, UA requiring hospitalization, revascularization and stroke

Secondary Prevention Algorithm



Secondary Prevention with Statins

- All patients with ASCVD should be treated with "High Intensity" Statin therapy **regardless** of baseline LDL-C (rosuvastatin 20-40 mg/d or atorvastatin 40-80 mg/d) but this is under prescribed:
  - Only 27% of 8762 MC beneficiaries with ASCVD who were prescribed a statin at discharge were actually prescribed a "High-intensity" statin.
  - Of those,
    - Only 23.1% Rx were actually filled if patients had not previously been on a statin
    - Only 9.4% Rx were actually filled if patients had previously been on "Moderate-intensity" statin)

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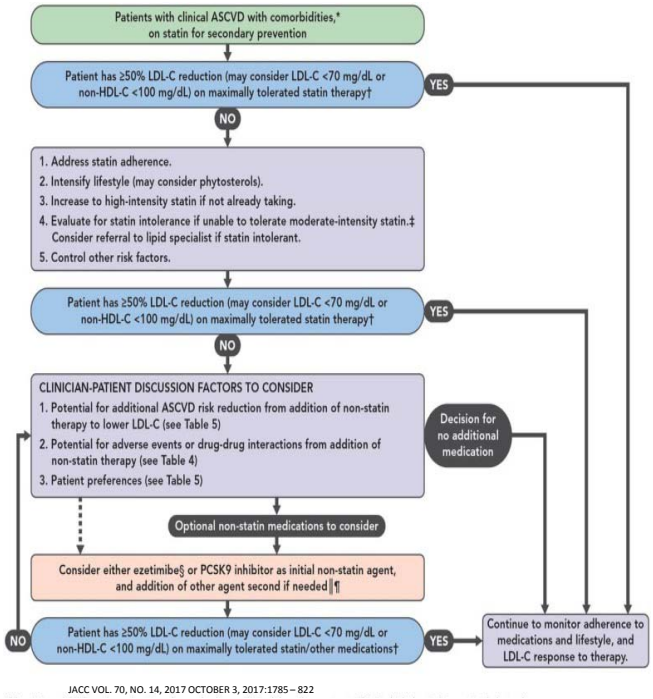

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Unified Definition of Statin Intolerance

- The inability to tolerate at least two different statins - one statin at the lowest starting average daily dose and the other statin at any dose.
- Associated with intolerable statin-related adverse effects or significant biomarker abnormalities not attributable to other conditions (drug-drug interactions, thyroid abnormalities, Vitamin D deficiency, etc).
- Symptoms or biomarker changes resolve/improve with discontinuation or dose reduction.

Statin Associated Side Effects (SASE)

- Hepatotoxicity
  - ↑LFT's 3%, Reversible liver injury 1:10,000, Liver failure 1:1,000,000
- New onset Diabetes
  - 10-20/10,000 patients/year
  - Net benefit still favors statin use. Patients who develop DM while on statin and remain on therapy have a 45% lower relative risk of MACE than those who do not take statin
- Stroke
  - Overall risk reduced, slight increased risk of hemorrhagic CVA
- Reduced Cognitive function
  - Post-marketing reports not confirmed in randomized trials
  - 29% reduction in risk of dementia with statin use
- Statin Myopathy

Statin Associated Muscle Symptoms (SAMS)

- Statin Associated Muscle Symptoms (SAMS), common
  - Myalgia – Muscle-discomfort, normal CK.
  - Myopathy – Muscle weakness +/- ↑CK
  - Myositis – Muscle inflammation
- Myonecrosis (symptoms + ↑CK)
  - Rare: 1/10,000 patients/year)
    - Mild – 3-10X, Moderate 10-50X, Severe >50X
- Rhabdomyolysis (myonecrosis with myoglobinuria or acute renal failure)
  - Extremely rare: 2-3/100,000 patients/year

Statin Associated Muscle Symptoms (SAMS)

- SAMS not definitely due to drug
- Meta-analysis of RCT's (130,000 patients)
  - 13.3% on statin discontinued drug
  - 13.9% on placebo discontinued drug
- Double-blind, Placebo-controlled, Crossover study of patients diagnosed with SAMS, given a "washout" period and assigned to restart statin or placebo
  - 36% had myalgias on statin
  - 30% has myalgias on placebo
- Suggests that muscle-related adverse events attributed to statins are not causally linked to the drug

Statin Intolerance - Consequences of cessation

- 105,329 MC beneficiaries
- 1741 (1.65%) had statin intolerance
- 55,567 (52.8%) had high statin adherence
- Compared to Statin Adherence, Statin Intolerance was associated with
  - 36% higher rate of recurrent MI
  - 43% higher rate of CHD events

Strategies to Increase Adherence

- Exclude other causes leading to intolerance
  - Hypothyroidism, Vitamin D deficiency, etc
- Statin Holiday
  - Many patients with SAMS/SASE may be able to tolerate as statin after washout
- Change statin (hydrophilic vs. lipophilic, different metabolic pathways)
- QOD dosing with long half-life agent
- Reduce dose to Moderate-intensity and add other agent:
  - ezetimibe, phytosterols, BAS, Fiber,
  - Limited outcomes data
- PCSK9 Inhibitors ($$$)
- OTC supplements (e.g., Co-Q-10) no clear benefit

What I Tell Patients

- Benefits of statins in High Risk patients are profound and incontrovertible
- Serious complications are exceedingly rare
- Side effects are common, but not definitely due to the medication
- Absolute Statin "Intolerance" is rare, many patients can tolerate statins when rechallenged

What I Tell Patients: Options for Statin Intolerant Patients

- 1. Take a statin and live with SASE's
  - With or without "add-on" therapy, dose adjustments, etc.
- 2. Don't take a statin and live with a significantly higher risk of CVA/MI and Death
- 3. Take a PCSK9 Inhibitor ($$$)
  - Many patients are willing to retry a statin when faced with the cost

Thank You