Ask the Experts: Clinical Case Studies Focusing on Non-statin Therapies for Treating Patients with Hypercholesterolemia

Presented as a Live Webinar

Wednesday, March 1, 2017
1:00 p.m. – 2:00 p.m. ET

www.ashpadvantage.com/go/pcsk9inhibitors

Planned by ASHP Advantage and supported by educational funding provided by Amgen and an independent educational grant by Sanofi US and Regeneron Pharmaceuticals..

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Activity Overview

This activity will focus on current issues related to the use of non-statin therapies for treating patients with hypercholesterolemia. The faculty will address the key issues and provide practice pearls for pharmacists.

The content for this activity is based on questions and comments from participants at a recent educational symposium on this topic. Time for additional questions from the webinar audience will be provided at the end of the presentation.

Learning Objectives

At the conclusion of this Application-based educational activity, participants should be able to

- Describe the evidence evaluating reduction in cardiovascular events with statin and non-statin combination therapy.
- Evaluate the use of non-statin therapies for the treatment of hypercholesterolemia in patients who cannot achieve desired LDL-C.
- Evaluate the use of non-statin therapies for the treatment of hypercholesterolemia in patients who report statin related muscle symptoms.

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Webinar Information

Visit www.ashpadvantage.com/go/pcsk9inhibitors/ate to find

- Webinar registration link
- Group viewing information and technical requirements
- CPE webinar processing information

Faculty

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University of Colorado Anschutz Medical Campus
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Joseph Saseen, Pharm.D., is Professor of Clinical Pharmacy and Family Medicine, and Vice-Chair of the Department of Clinical Pharmacy at the University of Colorado. He is Clinical Pharmacy Specialist in family medicine, Director of the PGY2 Ambulatory Care residency program and is a Board Certified Pharmacotherapy Specialist (BCPS) and Board Certified Ambulatory Care Pharmacist (BCACP).

Dr. Saseen received his Bachelor of Science degree in pharmacy and his Doctor of Pharmacy degree from the University at Buffalo. He completed a fellowship in ambulatory care research at the University of Colorado Health Sciences Center.

At the University of Colorado, Dr. Saseen participates in research related to the pharmacotherapy of chronic diseases (e.g., hypertension, dyslipidemia) and program grants related to the expansion of ambulatory care clinical services.

Dr. Saseen is a Fellow of the American Society of Health-System Pharmacists, American College of Clinical Pharmacy, and National Lipid Association. He is a past member and Chair of the Board of Pharmacy Specialties and is a board member of the National Lipid Association. He has several publications related to the pharmacotherapy of cardiovascular and was recipient of the American College of Clinical Pharmacy 2014 Education Award and the American Associations of Colleges of Pharmacy 2016 Teaching Innovations.

Ask the Experts: Clinical Case Studies Focusing on Non-statin Therapies for Treating Patients with Hypercholesterolemia

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Kim K. Birtcher, Pharm.D., is Clinical Professor at the University of Houston College of Pharmacy and clinical pharmacist at the Kelsey-Seybold Cardiology Clinic in Houston.

Dr. Birtcher received her Bachelor of Science degree in pharmacy and Master of Science degree in pharmacy administration from the University of Texas at Austin. She received her Doctor of Pharmacy degree from the University of Florida.

As a clinical pharmacist at the Kelsey-Seybold Cardiology Clinic in Houston, Texas, she is responsible for treating patients at the Secondary Prevention Lipid Clinic. Her teaching and research interests are in cardiovascular risk reduction and quality improvement initiatives.

Dr. Birtcher is a board certified pharmacotherapy specialist with additional qualifications in cardiology, a certified diabetes educator, and a clinical lipid specialist. She is an Associate of the American College of Cardiology (AACC) and a fellow of the National Lipid Association (FNLA). Dr. Birtcher is active in the American College of Cardiology (ACC), serving as the Co-Chair for the Cardiovascular Team Section's Working Group for Clinical Pharmacists. She is a member of the ACC/AHA Task Force on Clinical Practice Guidelines and the past Co-Chair of the LDL: Address the Risk Initiative launched by the ACC.

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The Changing Landscape of Hypercholesterolemia

The Emerging Role of Non-statin Therapies

Ask the Experts: Clinical Case Studies Focusing on Non-statin Therapies for Treating Patients with Hypercholesterolemia

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1.0 CPE

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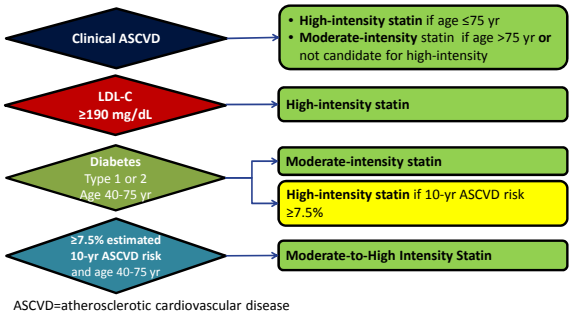
Learning Objectives

- Describe the evidence evaluating reduction in cardiovascular events with statin and non-statin combination therapy.
- Evaluate the use of non-statin therapies for the treatment of hypercholesterolemia in patients who cannot achieve desired LDL-C.
- Evaluate the use of non-statin therapies for the treatment of hypercholesterolemia in patients who report statin related muscle symptoms.

Case 1

- 40-year-old man being evaluated for lipid management
- PMH: heterozygous familial hypercholesterolemia (HeFH), MI 2 years ago, hypertension
- Meds: rosuvastatin 40 mg po daily, carvedilol 12.5 mg po twice daily, ramipril 10 mg po daily, aspirin 81 mg po daily
- States adherence to medications + lifestyle modifications (heart healthy diet, exercises four times weekly)
- LDL-C: Baseline 360 mg/dL, currently 170 mg/dL (↓ >50%)
- Was a 1-pack per day cigarette smoker prior to his MI, but no longer smokes

ACC/AHA 2013 Blood Cholesterol Guideline: Four ASCVD Statin Benefit Groups



ASCVD=atherosclerotic cardiovascular disease
ACC/AHA=American College of Cardiology/American Heart Association
Stone N et al. *Circulation*. 2014; 129(25 suppl 2):S1-45.

See enlargement, p. 15

ACC/AHA 2013 Blood Cholesterol Guideline: LDL-C ≥190 mg/dL

Class I Recommendations	Level of Evidence
If ≥21 years of age should be treated with statin therapy: • High-Intensity statin therapy unless contraindicated	B

Class IIa Recommendation	Level of Evidence
Reasonable to achieve at least a 50% LDL–C reduction.	B

Class IIb Recommendation	Level of Evidence
After the maximum intensity of statin therapy achieved, addition of a non-statin drug may be considered	C

Stone N et al. *Circulation*. 2014; 129(25 suppl 2):S1-45.

LDL-C ≥190 mg/dL

ACC/AHA 2013 Blood Cholesterol Guideline: Statin Intensity

High-Intensity	Moderate-Intensity	Low-Intensity
Daily dose lowers LDL–C on average, by ~ ≥ 50%	Daily dose lowers LDL–C on average, by ~ 30 to <50%	Daily dose lowers LDL–C on average, by <30%
Atorvastatin (40)–80 mg **Rosuvastatin 20** *(40)* **mg**	**Atorvastatin 10** *(20)* **mg** **Rosuvastatin** *(5)* **10 mg** **Simvastatin 20–40 mg** **Pravastatin 40** *(80)* **mg** **Lovastatin 40 mg** *Fluvastatin XL 80 mg* **Fluvastatin 40 mg bid** *Pitavastatin 2–4 mg*	*Simvastatin 10 mg* **Pravastatin 10–20 mg** **Lovastatin 20 mg** *Fluvastatin 20–40 mg* *Pitavastatin 1 mg*
Specific statins and doses are noted in **bold** that were evaluated in randomized controlled trials. Statins and doses that are approved by the U.S. FDA but were not tested in the RCTs reviewed are listed in italics.		

Stone NJ et al. *Circulation*. 2014; 129(25 suppl 2):S1-45.

NLA Recommendations – Part 1

Risk Category	Target Goal (mg/dL)		
	Non-HDL-C	LDL-C	Apo B
Low, Moderate, or High	<130	<100	<90
Very High	<100	<70	<80

- Primary Target: Non-HDL-C and LDL-C
- Secondary Optional Target: Apo B

NLA=National Lipid Association

Jacobson T et al. *J Clin Lipidol*. 2014; 8:473-88.

Which of the following changes to this patient's regimen will reduce his LDL-C value the most?

A. Add ezetimibe
B. Add omega-3 fatty acids
C. Add fenofibric acid
D. Switch rosuvastatin to atorvastatin 80 mg daily

Drugs Affecting Lipoprotein Metabolism

	LDL-C	HDL-C	TG
Statins	↓18-55%	↑5-15%	↓7-30%
Bile acid sequestrants (BAS)	↓15-30%	↑3-5%	↑0-10%
Nicotinic acid	↓5-25%	↑15-35%	↓20-50%
Fibric Acids	↓5-↑20%	↑10-20%	↓20-50%
Ezetimibe	↓13-20%	↑3-5%	↓5-11%
Omega-3 fatty acids	↓6-↑25%	↓5-↑7%	↓19-44%
PCSK9 inhibitors	↓40-72%	↑0-10%	↓0-17%

For LDL-C lowering

Primarily for hypertriglyceridemia

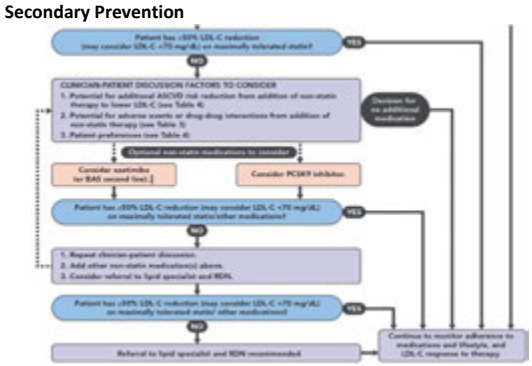
Jacobson TA et al. *J Clin Lipidol*. 2014; 8:473-88.
Shimada YJ, Cannon CP. *Eur Heart J*. 2016; 36:2415-24.

2016 ACC Expert Consensus Decision Pathway (ECDP) Role of Non-statin Therapies

- Endorsed the 2013 ACC/AHA 4 statin benefit group recommendations as initial approach
- Evaluate absolute LDL-C reduction as a "threshold" when considering addition of a non-statin
  - Non-HDL-C as a consideration for patients with diabetes mellitus

Lloyd-Jones D et al. *J Am Coll Cardiol*. 2016; 68:92-125.

Clinical ASCVD and Baseline LDL-C ≥ 190 mg/dL on Statin for Secondary Prevention

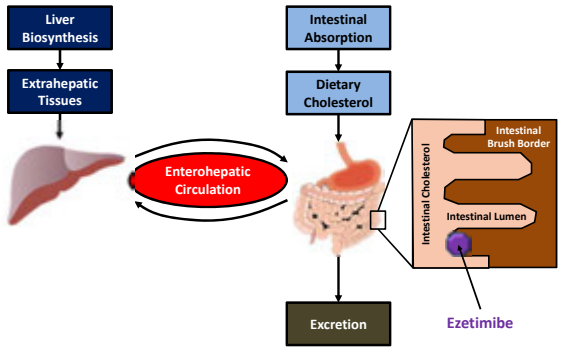


RDN=Registered dietitian nutritionist

Lloyd-Jones D et al. *J Am Coll Cardiol*. 2016; 68:92-125.

See enlargement, p. 15

Ezetimibe – Mechanism of Action



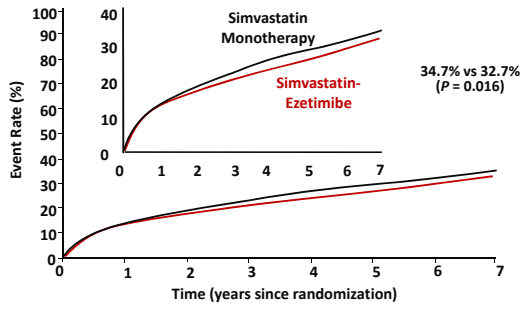
Gotto A et al. *Nat Clin Pract Cardiovasc Med*. 2006; 3:664–72.

IMPROVE-IT

- Double-blind randomized trial
- 18,144 patients with acute coronary syndrome
- Age ≥50 years with LDL-C 50-125 mg/dL (50-100 mg/dL if on therapy)
- Simvastatin or ezetimibe/simvastatin for 4.9 years
- Mean LDL-C values:
  - 69.9 mg/dL vs. 53.2 mg/dL

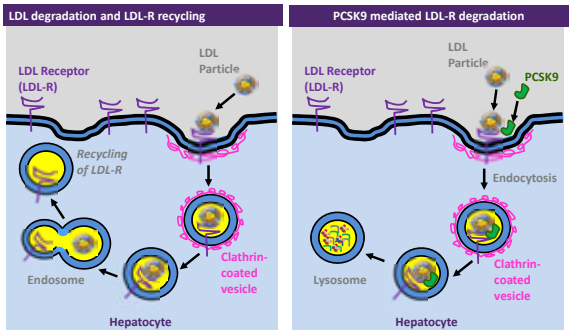
Cannon CP et al. *N Engl J Med*. 2015; 372:2387-97.

IMPROVE-IT: Primary Endpoint at Year 7



Cannon CP et al. *N Engl J Med*. 2015; 372:2387-97.

Proprotein Convertase Subtilisin/Kexin type 9 (PCSK9) Inhibitors



Lambert G et al. *J Lipid Research*. 2012; 53:2515-24.

See enlargement, p. 16

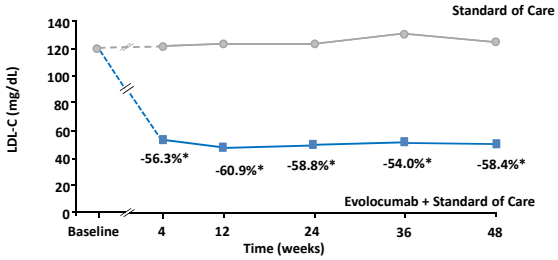
PCSK9 Inhibitors: Role in Therapy

- Alirocumab and Evolocumab FDA approval:
  - Adjunct to diet and maximally tolerated statin therapy for adults with heterozygous familial hypercholesterolemia (FH) or clinical atherosclerotic cardiovascular disease, who require additional lowering of LDL-C

	Dosing
Alirocumab	75 – 150 mg subcutaneously every 2 weeks
Evolocumab	140 mg subcutaneously every 2 weeks or 420 mg subcutaneously once monthly

Praluent (alirocumab) prescribing information. October 2015. http://products.sanofi.us/praluent/praluent.pdf. Repatha (evolocumab) prescribing information. July 2016. http://pi.amgen.com/united_states/repatha/repatha_pi_hcp_english.pdf.

Evolocumab (OSLER-1 and OSLER-2)



* All < 0.001

Sabatine M et al. *N Engl J Med*. 2015; 372:1500-9.

Which of the following is true regarding the addition of a PCSK9 inhibitor in this patient?

A. His insurance company should readily agree to approve a prior authorization because he has a history of ASCVD
B. There are no data demonstrating reduced CV events when added to statin therapy
C. It would be expected to significantly lower his LDL-C, triglycerides, and HDL-C
D. The LDL-C level is expected to be lowered by an additional 50 to 60%

Outcomes Studies with PCSK9 Inhibitors

- Several pending large-scale outcome trials
  - Preliminary Findings
    - Meta-analysis of 24 clinical trials (n=10,159)
      - Reduced MI: OR 0.49 (0.26-0.93)
      - Reduced all-cause mortality: OR 0.45 (0.23-0.86)
    - No increase in serious adverse events compared with no PCSK9 inhibitor

Navarese EP et al. *Ann Intern Med*. 2015;163:40-51.

GLobal Assessment of Plaque ReGression with a PCSK9 AntibOdy as Measured by IntraVascular Ultrasound (GLAGOV) Trial

- Phase 3, multicenter, double-blind, randomized, placebo-controlled trial
- Evaluated coronary atheroma volume in CAD patients (n=968) receiving optimized statin therapy
  - Randomized to evolocumab 420 mg or placebo subcutaneously monthly
- Primary Endpoint:
  - Percent atheroma volume from baseline to week 78 was significantly lower with evolocumab compared with placebo

Nicholls SJ et al. *JAMA*. 2016; 316:2373-84.

On the Horizon

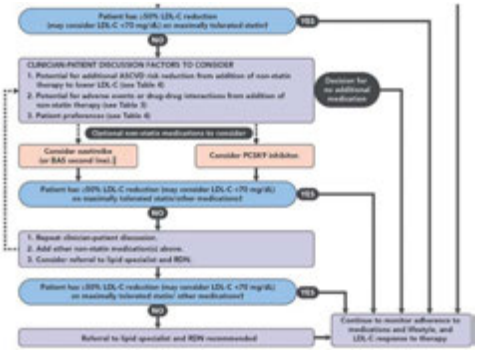
- FOURIER
  - ~27,500 ASCVD patients with LDL-C ≥ 70 mg/dL or non-HDL-C ≥ 100 mg/dL on optimized statin therapy
  - Evolocumab or placebo for up to 5 yr
  - Primary outcome: CV events

Update:

- Study stopped early due to achieving primary outcome
- Full results to be presented in March at the American College of Cardiology meeting

https://clinicaltrials.gov/ct2/show/NCT01764633

Clinical ASCVD and Baseline LDL-C ≥ 190 mg/dL on Statin for Secondary Prevention



Lloyd-Jones D et al. *J Am Coll Cardiol*. 2016; 68:92-125.

See enlargement, p. 16

Clinical ASCVD and Baseline LDL-C ≥ 190 mg/dL on Statin for Sec

- On high-intensity statin
- Achieved threshold?
  - Expected % LDL-C reduction of 50% is **met**, but LDL-C value of <70 mg/dL is **not met**
- Two non-statin therapies, PCSK9 inhibitor or ezetimibe, can be used
  - Both agents have evidence with statin therapy demonstrating further reduction in CV event risk
  - PCSK9 inhibitor is indicated for this patient
- Patient most likely to achieve an LDL-C < 70 mg/dL with a PCSK9 inhibitor plus statin therapy
- Patient may eventually need PCSK9 inhibitor and ezetimibe

Lloyd-Jones D et al. *J Am Coll Cardiol*. 2016; 68:92-125.

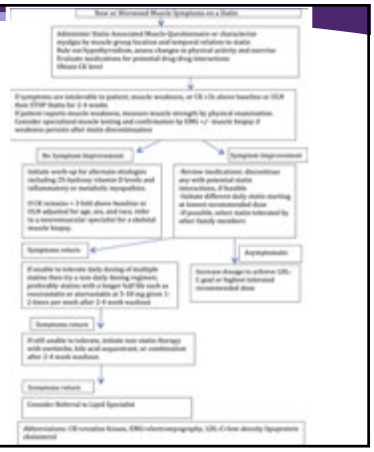
Case 2

- 52-year old man presents for follow-up in the clinic
- PMH: diabetes, hypertension
- Meds: atorvastatin 40 mg/day, metformin, verapamil
- States adherence to medications + lifestyle modifications (heart healthy diet, recently joined a tennis league)
- LDL-C: Baseline 174 mg/dL, currently 108 mg/dL (↓ 38%)
- Non-HDL-C: Currently 153 mg/dL
- 10-yr ASCVD risk > 7.5%
- Complains of muscle soreness in his back, neck, and lower extremities. Occurs 2-3 x per week. Limits his ability to exercise, but not activities of daily living.

According to the 2013 ACC/AHA Cholesterol Guideline, which of the following do you recommend?

A. Discontinue atorvastatin. Provide documentation in the chart that the patient is intolerant to statin therapy.
B. Switch atorvastatin to fluvastatin XL 80 mg/day. Provide documentation in the chart that the patient is intolerant to atorvastatin.
C. Switch atorvastatin to simvastatin 80 mg/day. Provide documentation in the chart that the patient is intolerant to atorvastatin.
D. Discontinue atorvastatin. Allow muscle symptoms to resolve. Restart atorvastatin 40 mg/day.

NLA Statin Muscle Safety Task Force



Rosenson RS et al. *J Clin Lipidol*. 2014; 8(3):s58-s71.

See enlargement, p. 17

NLA Statin Muscle Safety Task Force

Proposed Statin Myalgia Clinical Index Score

Clinical Symptoms (new or increased unexplained muscle symptoms)	
Regional distribution/pattern	
– Symmetric hip flexors/thigh aches	3
– Symmetric calf aches	2
– Symmetric upper proximal aches	2
– Non-specific asymmetric, intermittent	1
Temporal pattern	
– Symptom onset <4 weeks	3
– Symptom onset 4-12 weeks	2
– Symptom onset >12 weeks	1
De-challenge	
– Improves upon withdrawal (<2 weeks)	2
– Improves upon withdrawal (2-4 weeks)	1
Challenge	
– Same symptoms recur upon rechallenge <4 weeks	3
– Same symptoms recur upon rechallenge 4-12 weeks	1

Statin myalgia clinical index score
Probable 9-11
Possible 7-8
Unlikely <7

Rosenson RS et al. *J Clin Lipidol*. 2014;8(3):s58-71.

NLA Statin Intolerance Expert Panel

Statin intolerance

- Clinical syndrome
  - Characterized by inability to tolerate 2 statins (1 at lowest starting dose AND another at any daily dose)
  - Presence of objectionable symptoms (real or perceived) or abnormal lab values
    - Temporally related to statin treatment
    - Reversible upon statin discontinuation
    - Reproducible by rechallenge with other known determinants being excluded (such as hypothyroidism, interacting drugs, concurrent illnesses, significant changes in physical activity or exercise, underlying muscle disease)

Guyton JR et al. *J Clin Lipidol*. 2014; 8(3 Suppl):s72-81.

NLA Statin Intolerance Expert Panel

Recommendations to Clinicians

- Acknowledge that statin intolerance is real
- Frequency of statin-related muscle symptoms: 1% - 10%
- Statin-related muscle symptoms may include aching, stiffness, proximal motor weakness, fatigue, back pain
  - Severe myopathy with objective weakness and/or markedly elevated muscle enzymes is rare
- Decision on statin intolerance belongs to the patient
  - Based on subjective feelings, preferences, judgment
  - Aided by evaluation and communication with clinician

Guyton JR et al. *J Clin Lipidol*. 2014; 8(3 Suppl):s72-81.

NLA Statin Intolerance Expert Panel

Recommendations to Clinicians

- Clinicians should differentiate statin intolerance from "drug allergy"
  - Drug allergy implies substantial risk with rechallenge
  - Statin intolerance usually does not involve substantial risk for mortality or permanent disability
- **In most cases, clinicians and patients should attempt to keep some statin treatment**
  - May continue with doses or alternate statin to achieve less LDL-C reduction (eg., atorvastatin or rosuvastatin 5–10 mg taken once or twice a week may reduce LDL-C by 16–26%)

Guyton JR et al. *J Clin Lipidol*. 2014; 8(3 Suppl):s72-81.

NLA Statin Intolerance Expert Panel

Recommendations to Clinicians

- Clinicians may consider non-statin treatments of high LDL-C or non–HDL-C in statin-intolerant patients, with or without concomitant statin therapy
  - **Bile acid sequestrants, niacin, ezetimibe, fibrates, plant sterol esters or stanol esters, viscous fiber, and substitution of mono- or polyunsaturated fats for trans unsaturated or saturated fats in the diet**

Guyton JR et al. *J Clin Lipidol*. 2014; 8(3 Suppl):s72-81.

2013 ACC/AHA Cholesterol Guideline

Reasonable to evaluate and treat muscle symptoms (pain, tenderness, stiffness, cramping, weakness, fatigue) using algorithm:

- Before initiating statin therapy, ask about past or current muscle symptoms
- With unexplained muscle symptoms or fatigue, evaluate for rhabdomyolysis
- With mild-moderate muscle symptoms that develop during statin therapy
- Evaluate for other conditions that may cause muscle symptoms
  - Hypothyroidism, reduced renal or hepatic function, rheumatologic disorders, steroid myopathy, vitamin D deficiency, or primary muscle diseases

Stone N et al. Circulation. 2014; 129(25 suppl 2):S1-45.

2013 ACC/AHA Cholesterol Guideline

Reasonable to evaluate and treat muscle symptoms (pain, tenderness, stiffness, cramping, weakness, fatigue) using algorithm (cont'd):

- If muscle symptoms resolve and no contraindications, give same or lower dose of same statin to establish causal relationship between statin and muscle symptom.
- With causal relationship, stop statin. When symptoms resolve, use lower dose of different statin.
- When low dose is tolerated, gradually increase dose.
- If muscle symptoms or elevated creatine phosphokinase (CPK) do not resolve after 2 months without statin, consider other causes of muscle symptoms
- If the predisposing cause is resolved, resume statin at original dose

Stone N et al. *Circulation*. 2014; 129(25 suppl 2):S1-45.

ACC Expert Consensus Decision Pathway on the Role of Non-Statin Therapies

- Concurs with 2013 ACC/AHA Cholesterol Guideline methodology to evaluate muscle symptoms
- In addition, recommends rechallenging with > 2 - 3 statins
  - preferably ones that use different metabolic pathways and have different lipophilicity, and 1 prescribed at the lowest approved dose
- If patient cannot tolerate multiple statins at lowest dose, try alternative dosing strategies (e.g., long-acting statin 3 x week)
- "Non-statin therapies are not considered to be an alternative to evidence-based statin therapy unless statin intolerance has been systematically and rigorously evaluated and documented."

Lloyd-Jones D et al. *J Am Coll Cardiol*. 2016; 68:92-125.

Treatment Strategies in Patients with Statin Intolerance

<u>The Cleveland Clinic experience</u>

- Retrospective analysis of 1,605 patients referred for statin intolerance
  - 72.5% were able to tolerate a statin
  - Intermittent statin dosing (n=149) had lower LDL-C reduction compared with daily dosing (n=1014):
    - 21.3% vs 27.7% (P<0.04)
  - Trend toward a decrease in all-cause mortality at 8 years for patients on daily/intermittent statin dosing compared with those who discontinued statin (P=0.08)

Mampuya WM et al. *Am Heart J*. 2013;166:597-603.

Statin Intolerance

- 2013 ACC LDL Think Tank participants identified ***perceived*** statin intolerance as
  - One of the major barriers to statin adherence
  - A major cause of underutilization of statin therapy
- ACC developed the Statin Intolerance App to
  - Guide clinicians through the management of these patients
  - Helps keep appropriate patients on statin therapy to reduce CV risk

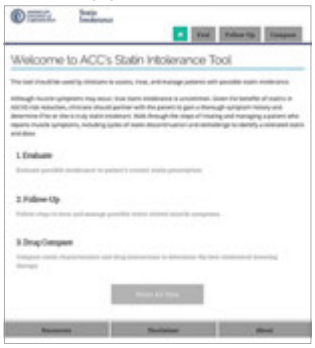
American College of Cardiology. ACC Statin Intolerance App. http://www.acc.org/StatinIntoleranceApp.

ACC Statin Intolerance App:

Overall Structure

The App contains three sections that can be used separately or in series, depending on the knowledge and needs of the clinician.

Evaluate
Follow-Up
Drug Compare



American College of Cardiology. ACC Statin Intolerance App. http://www.acc.org/StatinIntoleranceApp.

ACC Statin Intolerance App:

Evaluate

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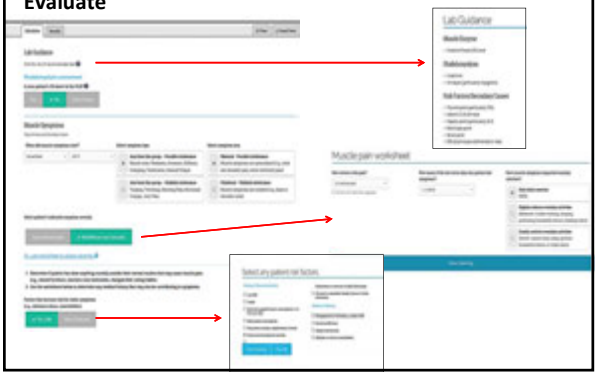
Evaluate



ACC Statin Intolerance App:

Evaluate

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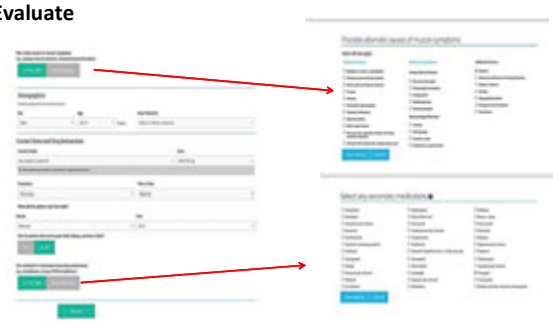

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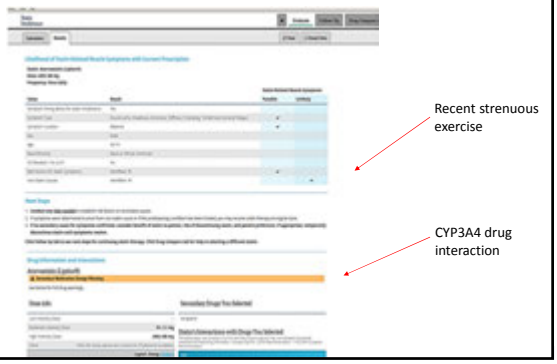
Evaluate



ACC Statin Intolerance App:
Follow-Up

ACC Statin Intolerance App:
Drug Compare

Case 2

- 52-year old man presents for follow-up in the clinic
- PMH: diabetes, HTN
- Meds: atorvastatin 40 mg/day, metformin, lisinopril
- States adherence to medications + lifestyle modifications (heart healthy diet, recently joined a tennis league)
- LDL-C: Baseline 174 mg/dL, currently 108 mg/dL (↓ 38%)
- Non-HDL-C: Currently 153 mg/dL
- 10-yr ASCVD risk > 7.5%
- Muscle symptoms resolved

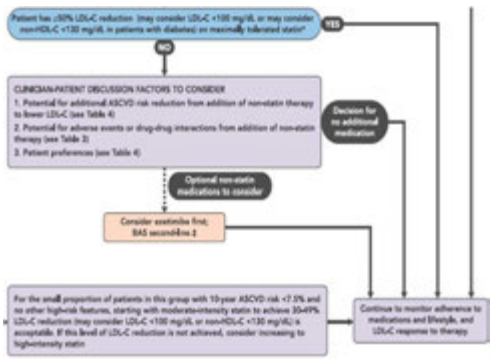
According to the ACC Expert Consensus Decision Pathway on the Role of Non-Statin Therapies, which of the following do you recommend?

A. Pt had less-than-anticipated response on moderate-intensity statin. Start ezetimibe.
B. Pt had anticipated response to high-intensity statin. Start colesevelam to lower LDL-C & A1c
C. Patient had less-than-anticipated response on high-intensity statin. Try alternate high-intensity statin therapy.
D. Clinician and pt should consider potential net ASCVD risk-reduction benefit of adding non-statin & pt preferences.

According to the ACC Expert Consensus Decision Pathway on the Role of Non-Statin Therapies, at which of the following thresholds may a non-statin be considered after maximizing the statin dose in this patient?

A. LDL-C < 70 mg/dL
B. LDL-C < 100 mg/dL
C. Non-HDL-C < 100 mg/dL
D. LDL-C reduction of at least 30% from baseline

Ages 40-75 (no Clinical ASCVD) + Diabetes



Lloyd-Jones D et al. *J Am Coll Cardiol*. 2016; 68:92-125.

See enlargement, p. 17

Ages 40-75 (no Clinical ASCVD) + Diabetes

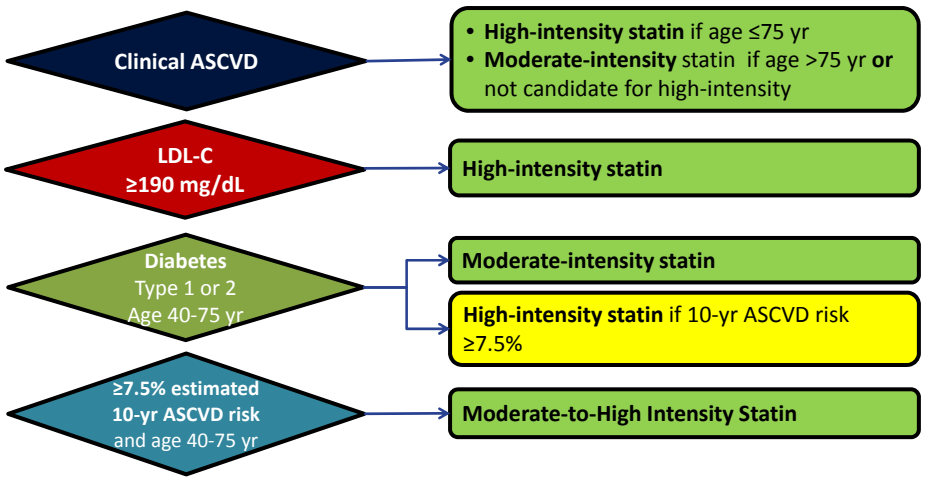
- Same initial clinical steps
- On moderate- or high-intensity statin
- Increase to high-intensity statin if needed
- Achieved threshold?
  - Expected % LDL-C reduction
    - Moderate-intensity: 30-<50%; high-intensity ≥50%
  - May consider LDL-C <100 mg/dL or non-HDL-C <130 mg/dL
- If not, consider adding ezetimibe (may consider BAS if ezetimibe intolerant + TG <300 mg/dL)
- PCSK9 inhibitor is not indicated

Lloyd-Jones D et al. *J Am Coll Cardiol*. 2016; 68:92-125.

Key Takeaways

- Evidence demonstrates that adding either ezetimibe or adding evolocumab to statin therapy in patients with ASCVD further reduces risk of CV events
- Patients with baseline LDL-C values ≥ 190 mg/dL and/or ASCVD may need the addition of a non-statin if certain LDL-C thresholds are not achieved
- Multiple strategies are available for the management of patients who report statin-related muscle symptoms to facilitate statin therapy

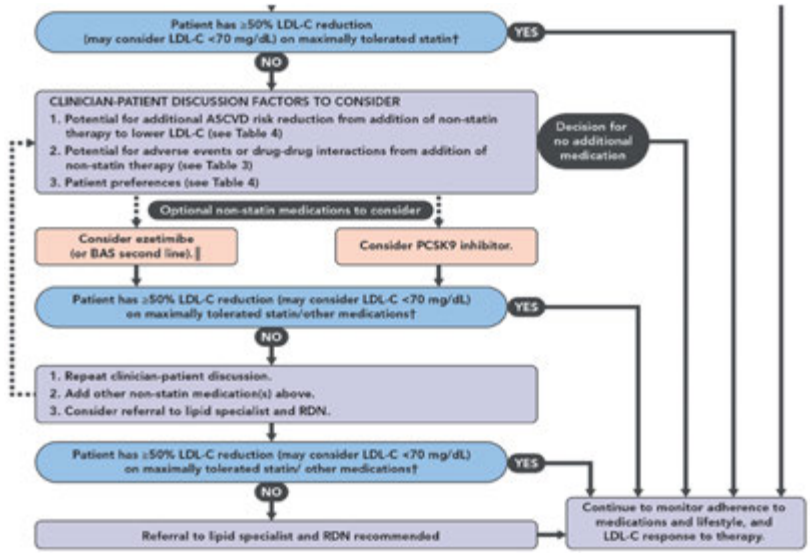
ACC/AHA 2013 Blood Cholesterol Guideline: Four ASCVD Statin Benefit Groups



ASCVD=atherosclerotic cardiovascular disease
ACC/AHA=American College of Cardiology/American Heart Association

Stone N et al. *Circulation*. 2014; 129(25 suppl 2):S1-45.

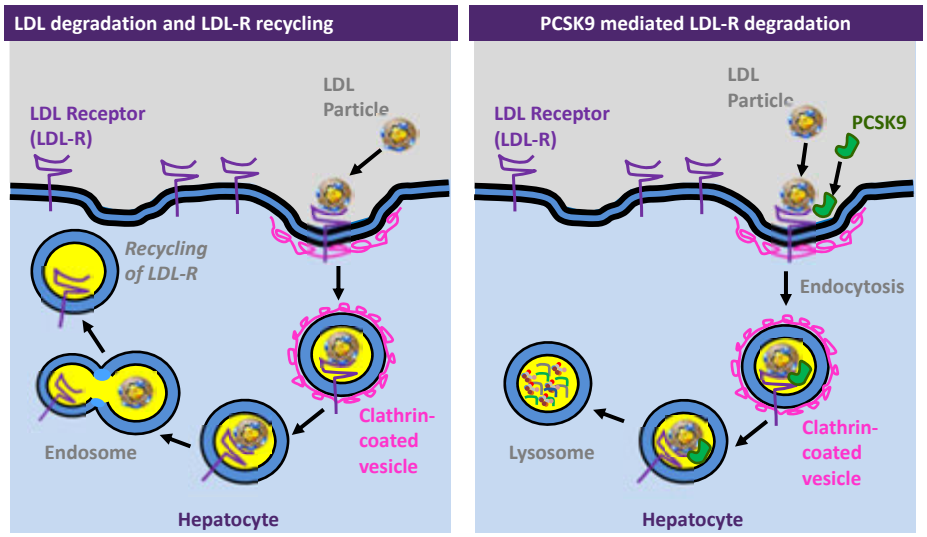
Clinical ASCVD and Baseline LDL-C ≥ 190 mg/dL on Statin for Secondary Prevention



RDN=Registered dietitian nutritionist

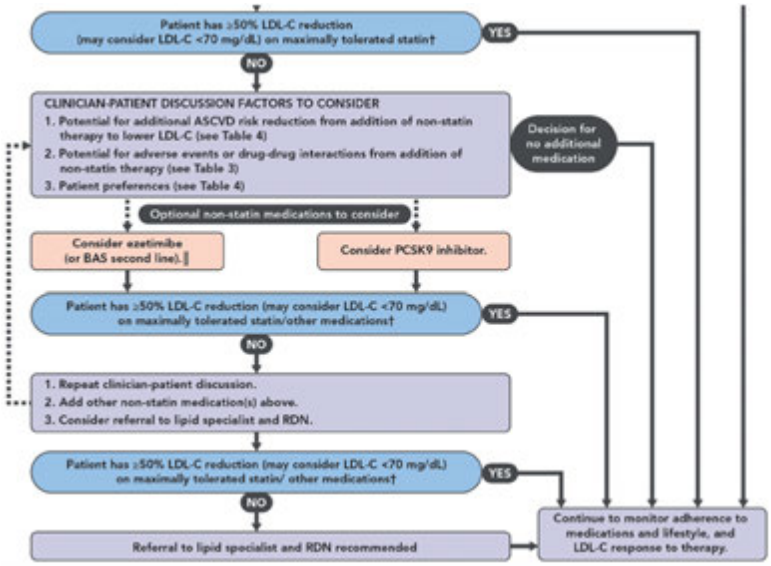
Lloyd-Jones D et al. *J Am Coll Cardiol*. 2016; 68:92-125.

Proprotein Convertase Subtilisin/Kexin type 9 (PCSK9) Inhibitors



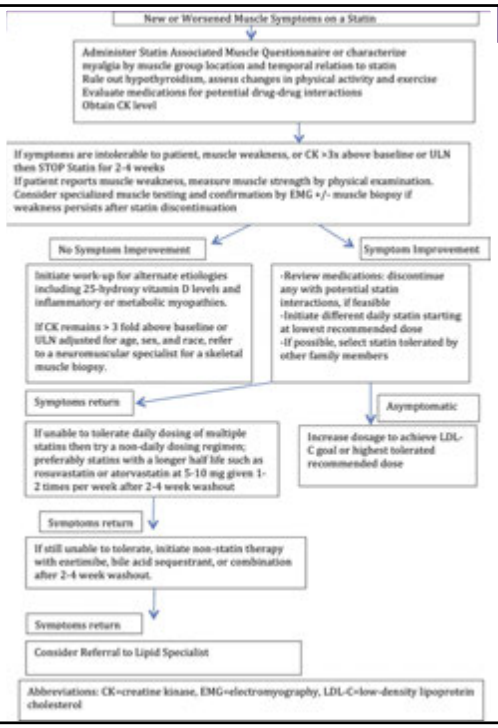
Lambert G et al. *J Lipid Research*. 2012; 53:2515-24.

Clinical ASCVD and Baseline LDL-C ≥ 190 mg/dL on Statin for Secondary Prevention



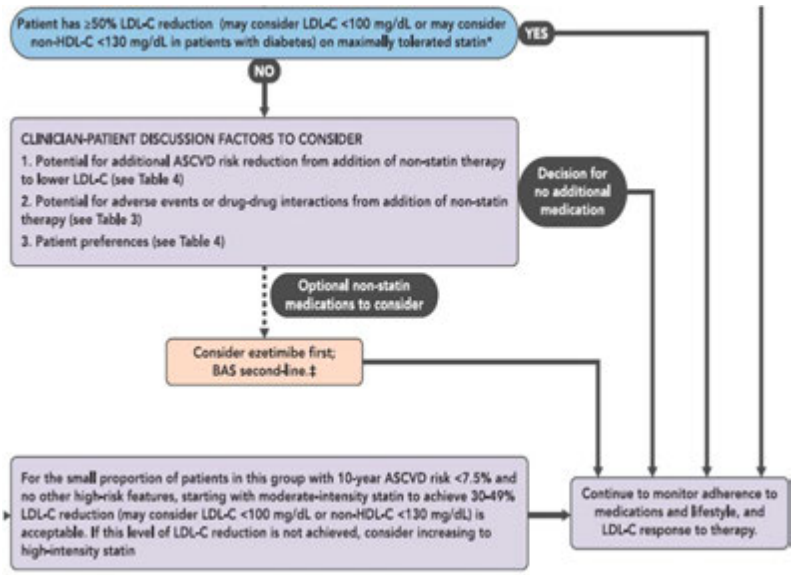
Lloyd-Jones D et al. *J Am Coll Cardiol*. 2016; 68:92-125.

NLA Statin Muscle Safety Task Force



Rosenson RS et al. *J Clin Lipidol*. 2014; 8(3):s58-s71.

Ages 40-75 (no Clinical ASCVD) + Diabetes



Lloyd-Jones D et al. *J Am Coll Cardiol*. 2016; 68:92-125.

Self-Assessment Case Studies

Case 1: A 40-year-old man being evaluated for lipid management

- PMH: heterozygous familial hypercholesterolemia (HeFH), MI 2 years ago, hypertension
- Meds: rosuvastatin 40 mg po daily, carvedilol 12.5 mg po twice daily, ramipril 10 mg po daily, aspirin 81 mg po daily
- States adherence to medications + lifestyle modifications (heart healthy diet, exercises four times weekly)
- LDL-C: Baseline 360 mg/dL, currently 170 mg/dL (↓ >50%)
- Was a 1-pack per day cigarette smoker prior to his MI, but no longer smokes

1. Which of the following changes to this patient's regimen will reduce his LDL-C value the most?
   a. Add ezetimibe
   b. Add omega-3 fatty acids
   c. Add fenofibric acid
   d. Switch rosuvastatin to atorvastatin 80 mg daily

2. Which of the following is true regarding the addition of a PCSK9 inhibitor in this patient?
   a. His insurance company should readily agree to approve a prior authorization because he has a history of ASCVD
   b. There are no data demonstrating reduced CV events when added to statin therapy
   c. It would be expected to significantly lower his LDL-C, triglycerides, and HDL-C
   d. The LDL-C level is expected to be lowered by an additional 50 to 60%

Case 2, part 1: A 52-year old man presents for follow-up in the clinic

- PMH: diabetes, hypertension
- Meds: atorvastatin 40 mg/day, metformin, verapamil
- States adherence to medications + lifestyle modifications (heart healthy diet, recently joined a tennis league)
- LDL-C: Baseline 174 mg/dL, currently 108 mg/dL (↓ 38%)
- Non-HDL-C: Currently 153 mg/dL
- 10-yr ASCVD risk > 7.5%
- Complains of muscle soreness in his back, neck, and lower extremities. Occurs 2-3 x per week. Limits his ability to exercise, but not activities of daily living.

3. According to the 2013 ACC/AHA Cholesterol Guideline, which of the following do you recommend?
    a. Discontinue atorvastatin. Provide documentation in the chart that the patient is intolerant to statin therapy.
    b. Switch atorvastatin to fluvastatin XL 80 mg/day. Provide documentation in the chart that the patient is intolerant to atorvastatin.
    c. Switch atorvastatin to simvastatin 80 mg/day. Provide documentation in the chart that the patient is intolerant to atorvastatin.
    d. Discontinue atorvastatin. Allow muscle symptoms to resolve. Restart atorvastatin 40 mg/day.

Case 2, part 2: 52-year old man presents for follow-up in the clinic

- PMH: diabetes, HTN
- Meds: atorvastatin 40 mg/day, metformin, lisinopril
- States adherence to medications + lifestyle modifications (heart healthy diet, recently joined a tennis league)
- LDL-C: Baseline 174 mg/dL, currently 108 mg/dL (↓ 38%)
- Non-HDL-C: Currently 153 mg/dL
- 10-yr ASCVD risk > 7.5%
- Muscle symptoms resolved

4. According to the ACC Expert Consensus Decision Pathway on the Role of Non-Statin Therapies, which of the following do you recommend?
    a. Pt had less-than-anticipated response on moderate-intensity statin. Start ezetimibe.
    b. Pt had anticipated response to high-intensity statin. Start colesevelam to lower LDL-C & A1c
    c. Patient had less-than-anticipated response on high-intensity statin. Try alternate high-intensity statin therapy.
    d. Clinician and pt should consider potential net ASCVD risk-reduction benefit of adding non-statin & pt preferences.
5. According to the ACC Expert Consensus Decision Pathway on the Role of Non-Statin Therapies, at which of the following thresholds may a non-statin be considered after maximizing the statin dose in this patient?
    a. LDL-C < 70 mg/dL
    b. LDL-C < 100 mg/dL
    c. Non-HDL-C < 100 mg/dL
    d. LDL-C reduction of at least 30% from baseline