The Changing Landscape of Hypercholesterolemia: The Emerging Role of Non-statin Therapies

Presented as a Midday Symposium and Live Webinar at the
51st ASHP Midyear Clinical Meeting and Exhibition

Tuesday, December 6, 2016
Las Vegas, Nevada

http://www.ashpadvantage.com/go/pcsk9inhibitors

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Please be advised that this activity is being audio and/or video recorded for archival purposes and, in some cases, for repurposing of the content for enduring materials.

Agenda

11:30 a.m.-11:35 a.m.
Welcome and Introductions
Joe Saseen, Pharm.D., BCPS, BCACP, FASHP, FCCP, *Activity Chair*

11:35a.m.-12:00 p.m.
Overview of Non-statin Therapies in the Management of Hypercholesterolemia: New Guideline Recommendations and Expert Consensus
Joe Saseen, Pharm.D., BCPS, BCACP, FASHP, FCCP

12:00 p.m.-12:50 p.m.
Case Studies in the Management of Hypercholesterolemia: The Role of Non-statin Therapies
Joe Saseen, Pharm.D., BCPS, BCACP, FASHP, FCCP
Kim Birtcher, M.S, Pharm.D, AACC, FNLA, BCPS-AQ Cardiology, CDE, CLS

12:50 p.m. -01:00 p.m.
Faculty Discussion and Audience Questions
All Faculty

Faculty

Joseph Saseen, Pharm.D., BCPS, BCACP, *Activity Chair*
Professor & Vice Chair
University of Colorado Anschutz Medical Campus
Aurora, Colorado

Kim K. Birtcher, Pharm.D, AACC, FNLA, BCPS-AQ Cardiology, CDE, CLS
Clinical Professor
University of Houston College of Pharmacy
Clinical Pharmacist
Kelsey-Seybold Cardiology Clinic
Houston, Texas

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Activity Overview

Given changing approaches to the treatment of hypercholesterolemia, which includes patients with familial hypercholesterolemia or clinical atherosclerotic cardiovascular disease, this educational activity will review current and upcoming guideline recommendations and expert consensus for the treatment of this disorder in adults. With the recent approval of two PCSK9 inhibitors, the mechanism of action, indications, and clinical trial data on efficacy of these agents will be reviewed. Special considerations necessary for the procurement, storage, and administration of the PCSK9 inhibitors will also be described. Case studies will illustrate the appropriate use of non-statin therapies in the management of hypercholesterolemia.

Learning Objectives

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

- Apply new guideline and expert consensus recommendations for the treatment of hypercholesterolemia in adults.
- Compare and contrast the mechanism of action of the PCSK9 inhibitors with statins and other non-statin drugs for the treatment of hypercholesterolemia.
- Analyze the potential role of non-statin drug therapies in the management of patients with hypercholesterolemia, including patients with familial hypercholesterolemia.
- Describe the role of the pharmacist in managing patients with hypercholesterolemia.

Continuing Education Accreditation

The American Society of Health-System Pharmacists is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education.

This activity provides 1.5 hours (0.15 CEUs – no partial credit) of continuing pharmacy education credit.

Live Activity ACPE #: 0204-0000-16-471-L01-P
On-Demand Activity ACPE #: 0204-0000-16-471-H01-P

Complete instructions for processing continuing education credit online are listed on the last page.

Webinar Information

Visit **http://www.ashpadvantage.com/go/pcsk9inhibitors/virtual** to find:

- Webinar registration link
- Group viewing information and technical requirements

Additional Educational Opportunities on Hypercholesterolemia Coming in 2017

- **Ask the Experts webinar** – Faculty will explore issues raised by participant questions in today's symposium (1 hour CPE)
- **e-Newsletter** – Featuring updates on new and emerging information and ideas for incorporating information from this symposium into practice
- **Web-based activity** - Based on today's live symposium (1.5 hours of CPE, *please note that individuals who claim CPE credit for the live symposium or webinar are ineligible to claim credit for the web-based activity*)

For more information and to sign up to receive e-mail updates about this educational series, visit

http://www.ashpadvantage.com/go/pcsk9inhibitors

Faculty Biographies

Joseph Saseen, Pharm.D., BCPS, BCACP, FASHP, FCCP
Professor, Departments of Clinical Pharmacy and Family Medicine
Vice-Chair, Department of Clinical Pharmacy
University of Colorado School of Pharmacy
Aurora, Colorado

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.

The Changing Landscape of Hypercholesterolemia: The Emerging Role of Non-statin Therapies

Kim K. Birtcher, Pharm.D, M.S., BCPS-AQ Cardiology, CLS, CDE, AACC, FNLA
Professor
University of Houston College of Pharmacy
Clinical Pharmacist
Kelsey-Seybold Clinic
Houston, Texas

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.

The Changing Landscape of Hypercholesterolemia

The Emerging Role of Non-statin Therapies

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Kim K. Birtcher, Pharm.D., M.S., BCPS-AQ Cardiology, CDE, CLS, AACC, FNLA
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1.5 CPE

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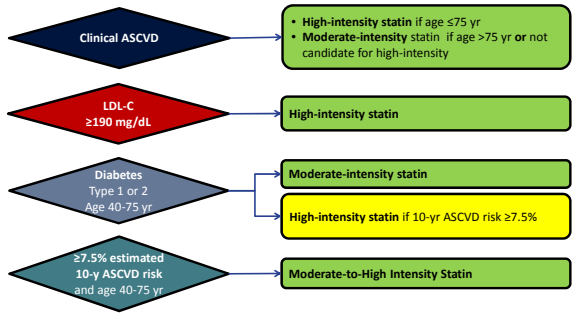
Learning Objectives

- Apply new guideline and expert consensus recommendations for the treatment of hypercholesterolemia in adults.
- Compare and contrast the mechanism of action of the PCSK9 inhibitors with statins and other non-statin drugs for the treatment of hypercholesterolemia.
- Analyze the potential role of non-statin drug therapies in the management of patients with hypercholesterolemia, including patients with familial hypercholesterolemia.
- Describe the role of the pharmacist in managing patients with hypercholesterolemia.

Overview of Non-statin Therapies in the Management of Hypercholesterolemia: New Guideline and Expert Consensus Decision Pathway

Joseph Saseen, Pharm.D., BCPS, BCACP, FASHP, FCCP, CLS
Activity Chair
Professor and Vice Chair
University of Colorado Anschutz Medical Campus
Aurora, Colorado

Four ASCVD Statin Benefit Groups



ASCVD=atherosclerotic cardiovascular disease

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

ACC/AHA Format for Evidence-Based Recommendations

Class of Recommendations

I:	Benefits >>> Risk
IIa:	Benefits >> Risk
IIb:	Benefit ≥ Risk

Level of Evidence

A:	Multiple populations; data from multiple RCTs or meta-analyses
B:	Limited populations and single RCT or non-controlled studies
C:	Very limited populations; consensus opinion

ACC/AHA=American College of Cardiology/American Heart Association
RCT=Randomly controlled trial

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

ACC/AHA 2013 Blood Cholesterol Guideline: ASCVD

Class I Recommendations	Level of Evidence
High-Intensity statin therapy should be initiated or continued as first line therapy in men and women ≤ 75 years of age, unless contraindicated	A
If high-Intensity statin therapy is contraindicated or when characteristics predisposing to statin-associated adverse effects are present, **Moderate-Intensity** statin therapy should be the second option if tolerated	A

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

Clinical ASCVD

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.

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

2013 ACC/AHA Guidelines Preamble

"Guidelines attempt to define practices that meet the needs of patients in most circumstances and are not a replacement for clinical judgment.

The ultimate decision about care of a particular patient must be made by the healthcare provider and patient in light of the circumstances presented by that patient.

As a result, situations might arise in which deviations from these guidelines may be appropriate."

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

NLA Recommendations – Part 1

Risk Category	Criteria
Low	• ≤1 major ASCVD risk factor • Consider other risk factors if known
Moderate	• 2 major ASCVD risk factors • Consider quantitative risk scoring using a 10-year risk calculator, or other risk indicators
High	• ≥3 major ASCVD risk factors • Diabetes mellitus (type 1 or 2) with: - ≤1 other major ASCVD risk factor, and - No evidence of end organ damage • Chronic kidney disease stage 3B or 4 • LDL-C ≥190 mg/dL • Quantitative risk score reaching the high-risk threshold
Very High	• ASCVD • Diabetes mellitus (type 1 or 2) with: - ≥2 other major ASCVD risk factors, and - Evidence of end organ damage

NLA=National Lipid Association

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

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

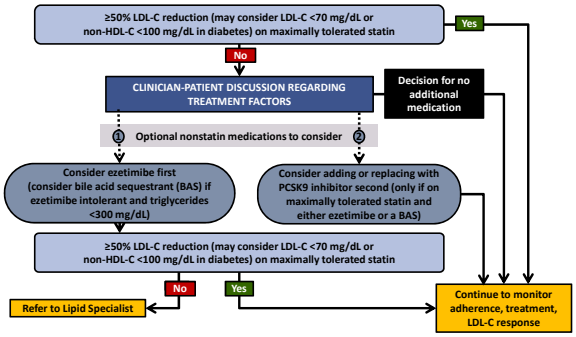
Jacobson T et al. *J Clin Lipidol*. 2014; 8:473-88.

2016 ACC Expert Consensus Decision (ECDP) Pathway 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(1):92-125.

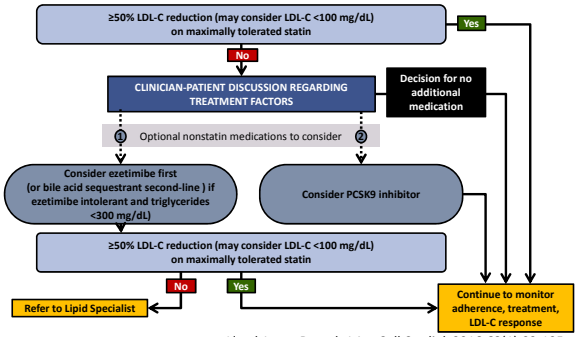
2016 ACC ECDP
Clinical ASCVD with Comorbidities



Lloyd-Jones D et al. *J Am Coll Cardiol*. 2016;68(1):92-125.

See enlargement, p. 30

2016 ACC ECDP
Without ASCVD, Baseline LDL-C ≥ 190 mg/dL



Lloyd-Jones D et al. *J Am Coll Cardiol*. 2016;68(1):92-125.

See enlargement, p. 30

2016 ACC ECDP: Summary

- Non-statin only after maximally tolerated statin
  - Ezetimibe (or bile acid sequestrant) first followed by PCSK9 inhibitors
  - Niacin not recommended
- PCSK9 inhibitors only in ASCVD and/or baseline LDL-C ≥190 mg/dL
- Actual LDL-C value (or %LDL-C reduction achieved) as the threshold:
  - <70 mg/dL (or 50% reduction) if ASCVD with comorbidities or baseline LDL-C ≥190 mg/dL
  - otherwise <100 mg/dL

Lloyd-Jones D et al. *J Am Coll Cardiol*. 2016;68(1):92-125.

Drugs Affecting Lipoprotein Metabolism

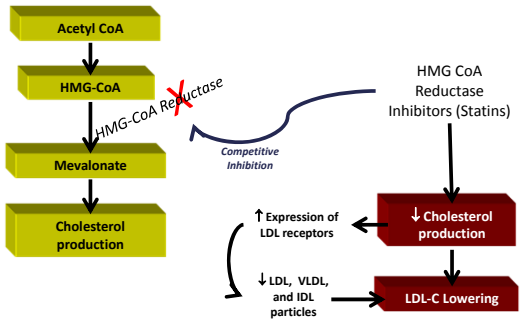
	LDL-C	HDL-C	TG
Statins	↓18-55%	↑5-15%	↓7-30%
Bile acid sequestrants	↓15-30%	↑3-5%	↑0-10%
Nicotinic acid	↓5-25%	↑15-35%	↓20-50%
Fibric Acids	↓5-↑20%	↑10-20%	↓20-50%
Ezetimibe	↓13-20%	↑3-5%	↓5-11%
Omega-3 fatty acids	↓6-↑25%	↓5-↑7%	↓19-44%
PCSK9 inhibitors	↓40-72%	↑0-10%	↓0-17%

For LDL-C lowering

Primarily for hypertriglyceridemia

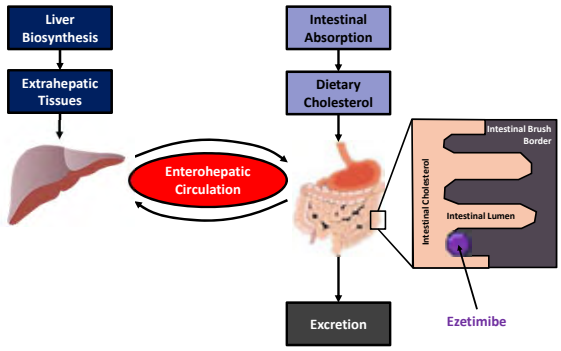
Jacobson TA et al. *J Clin Lipidol*. 2014; 8:473-88.
Shimada YJ, Cannon CP. *Eur Heart J*. 2016; 36:2415-24.

Statins



VLDL=very-low-density lipoprotein, IDL=intermediate-density lipoprotein

Ezetimibe – Mechanism of Action



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

Cholesterol Absorption Inhibitor

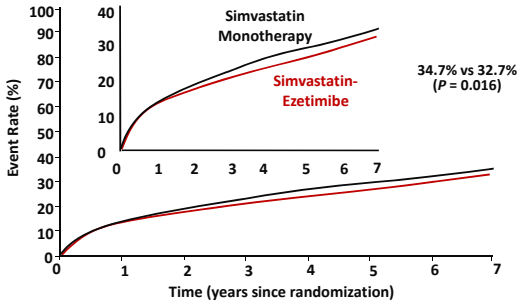
- Combination with statin for additional LDL-C lowering
- Alternative treatment in statin-resistant patients
- Ezetimibe is the only available agent
- Provides ~ 18% reduction in LDL-C
- Overall safe and well tolerated
- Outcomes data from IMPROVE-IT

IMPROVE-IT

- Double-blind randomized trial in 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.

Heartwire from Medscape

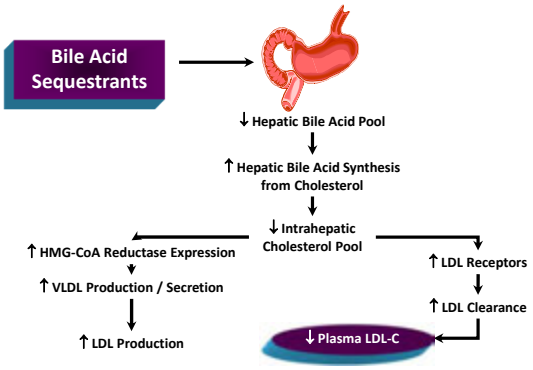
FDA Advisors: Reject Secondary-Prevention Ezetimibe Indication

Deborah Brauser
December 14, 2015

SILVER SPRING, MD (***UPDATED***) — The Endocrinologic and Metabolic Drugs Advisory Committee of the US Food and Drug Administration (FDA) voted 10 to 5 against recommending the expanded use of ezetimibe (*Zetia*, Merck) by adding it to statin therapy for reduction of cardiovascular events in patients with coronary heart disease

http://www.medscape.com/viewarticle/855958?nlid=93603_2562&src=wnl_edit_medp_card&uac=397755MJ&spon=2&impID=921002&faf=1

Bile Acid Sequestrants

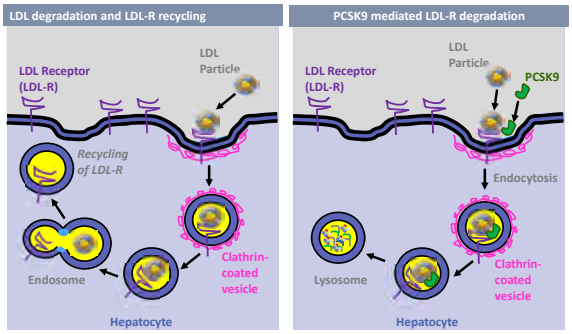


Bile Acid Sequestrants: Role in Therapy

- Combination with statin for additional LDL-C lowering (familial hypercholesterolemia)
- Alternative treatment in statin-resistant patients
- Non-cholesterol lowering use for lowering A1C (colesevelam) and other off-label uses
- CV Event Reduction:
  - LRC-Primary Prevention Trial (n=3086):
    - Cholestyramine reduced fatal CHD/non-fatal MI by 19% vs. placebo ($p<0.05$)

Lipid Research Clinics Coronary Primary Prevention Trial. *JAMA*. 1984; 251:351-64.

Proprotein Convertase Subtilisin/Kexin type 9 (PCSK9) Inhibitors



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

See enlargement, p. 31

PCSK9 Inhibitors: Role in Therapy

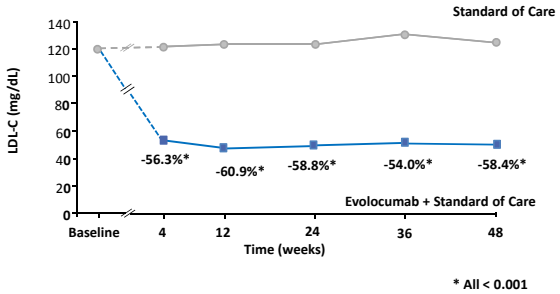
- Alirocumab and Evolocumab FDA approval:
  - Adjunct to diet and maximally tolerated statin therapy for adults with heterozygous familial hypercholesterolemia (FH) or clinical atherosclerotic cardiovascular disease, who require additional lowering of LDL-C
  - Evolocumab also approved for homozygous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

	Dosing
Alirocumab	75 – 150 mg subcutaneous every 2 weeks
Evolocumab	140 mg subcutaneous every 2 weeks or 420 mg subcutaneous once monthly in homozygous FH patients

- Use in statin intolerance is debated and evolving

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.

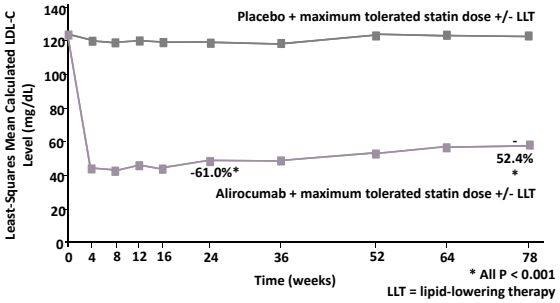
Evolocumab (OSLER-1 and OSLER-2)



* All < 0.001

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

Alirocumab (ODYSSEY LONGTERM)



* All P < 0.001
LLT = lipid-lowering therapy

Robinson JG, et al. *N Engl J Med*. 2015; 372(16):1489-99.

Alirocumab (ODYSSEY LONGTERM) Safety Analysis

Summary of Adverse Events (AE)	Alirocumab (*n* = 1,550)	Placebo (*n* = 788)	*P* Value
Serious Adverse Events	290 (18.7%)	154 (19.5%)	0.66
• AE leading to discontinuation	111 (7.2%)	46 (5.8%)	0.26
• AE leading to death	8 (0.5%)	10 (1.3%)	0.08
General allergic reaction events	156 (10.1%)	75 (9.5%)	0.71
Local injection site reactions	91 (5.9%)	33 (4.2%)	0.10
Neurologic events	65 (4.2%)	35 (4.4%)	0.83
Neurocognitive events	18 (1.2%)	4 (0.5%)	0.17

Among patients who received alirocumab, 575 (37.1%) had a calculated LDL-C level of <25 mg/dL at 2 consecutive measurements. Rates of AEs were similar to those in the overall alirocumab group.

Robinson J et al. *N Engl J Med*. 2015; 372:1489-99.

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

Amgen news release. September 20, 2016. http://www.amgen.com/media/news-releases/2016/09/amgen-announces-positive-topline-results-from-phase-3-glagov-imaging-study-of-repatha-evolocumab/

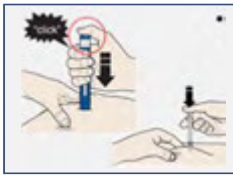
PCSK9 Inhibitor: Monitoring and Education

- Measure LDL-C levels within 4-8 weeks after initiating or titrating to assess response and adjust dose if needed
- Missed dose education
  - Instruct patient to administer injection within 7 days after the missed dose, then resume original schedule
  - If missed dose not administered within 7 days, instruct patient to wait until the next dose on the original schedule
- If allergic reactions appear, discontinue and treat patient according to standard of care

PCSK9 Inhibitors: Injection Instructions

- Do not pull the cap off of the syringe/autopen until you are ready to inject the medication
- Rotate injection sites
- Assistance may be needed when injecting into arms
- Make sure the pen or syringe is completely empty before removing needle from skin
- The time required for injection of the entire dose may be longer than that for other injectable medicines

PCSK9 Inhibitor Injection Devices



- **Traditional**
  - Injection every 2 weeks
  - Single-use, prefilled autoinjector or syringe
  - Delivers 75-140 mg/mL dose subcutaneously for up to 15 seconds
  - Patient self-injects medicine

- **Recently Approved (evolocumab only)**
  - Injection once a month
  - Single-use on-body infusor with prefilled cartridge
  - Delivers 420 mg/3.5 mL dose for up to 9 minutes
  - Adheres to body, device injects medicine

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.

PCSK9 Inhibitors: Storage and Handling

- Store unused syringes in refrigerator between 36°F to 46°F in outer carton to protect from light
- Do not freeze, do not expose the pen or syringe to extreme heat or direct sunlight, do not shake
- Should be allowed to warm to room temperature for 30-40 minutes before use
- Alirocumab:
  - Do not keep at room temperature for more than 24 hours
- Evolocumab:
  - May be stored at room temperature if used within 30 days

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

Specialty Pharmacies

- Stock biologic medications with restricted use, are high cost, or have safety concerns
- Typically specialty pharmacy services:
  - Home delivery or select in-store pickup for patients
  - Help with prior authorizations and appeals
  - Some may use electronic prior authorization programs, such as www.covermymeds.com
- Train patients to self-inject drugs
- Send patient reminders, call regarding refills
- Enroll patients in patient assistance programs

American Pharmacists Association. www.pharmacist.com/specialty-pharmacy (accessed 2016 Apr 20).

Targeted Populations for PCSK9 Inhibitors

Clinical ASCVD

Familial Hypercholesterolemia (FH)

- CV events seen despite aggressive LDL-lowering therapy in many patients, especially in FH
- Other options do not provide robust LDL-C reduction
- Some other options are inconvenient, not well tolerated and more costly than PCSK9 inhibitors


THE PRESENT AND FUTURE

COUNCIL PERSPECTIVES

The Role of the Clinical Pharmacist in the Care of Patients With Cardiovascular Disease

Optimization of drug use **Avoidance of adverse drug events**
Transitional care activities **Medication reconciliation**
Patient education

Dunn SP et al. *J Am Coll Cardiol*. 2015; 66(19):2129-39.

2015 ACC Health Policy Statement on Cardiovascular Team-Based Care and the Role of Advanced Practice Providers

- Encourages the exploration of collaborative care models that should enable team members to optimize their education, training, experience, and talent
- Consistent with the mission of ACC "to transform cardiovascular care and improve heart health"
- Aligned to achieve the triple aim of improved care, improved population health, and lower costs

Brush JE et al. *J Am Coll Cardiol*. 2015; 65(19):2118–36.

Case Studies in the Management of Hypercholesterolemia: The Role of Non-statin Therapies

Kim K. Birtcher, Pharm.D., M.S., BCPS-AQ Cardiology, CLS, CDE, AACC, FNLA
Clinical Professor
University of Houston College of Pharmacy
Houston, Texas

Case 1

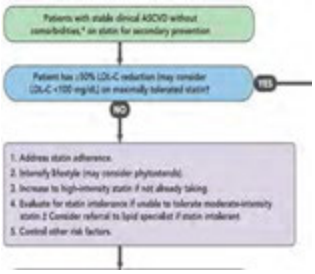
49-year old man presents for follow-up in the clinic

- PMH: hypercholesterolemia, chronic stable angina
- States adherence to atorvastatin 20 mg/day (and other meds) + lifestyle modifications
- BMI 32 kg/m^2 (stable for 3 years)
- LDL-C has ↓ 42% from baseline
- LDL-C = 130 mg/dL

Which of the following do you recommend?

A. Pt is intolerant to statin therapy. Stop atorvastatin.
B. Pt had less-than-anticipated response on moderate-intensity statin. Start ezetimibe.
C. Pt had anticipated response to moderate-intensity statin. Try alternate high-intensity statin therapy prior to adding non-statin.
D. Clinician and pt should consider potential net ASCVD risk-reduction benefit of adding non-statin & pt preferences.

Patients with Stable Clinical ASCVD Without Comorbidities



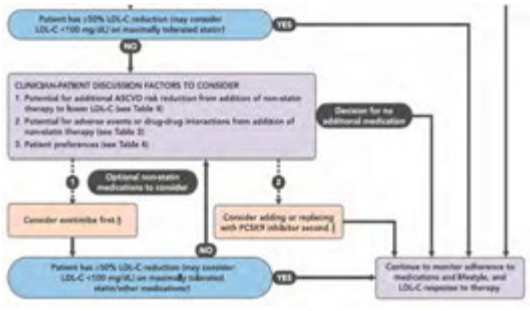
Comorbidities
1. Diabetes mellitus
2. Recent (<3 mo) acute ASCVD event
3. ASCVD event while on statin
4. Baseline LDL-C ≥190 mg/dL
5. Uncontrolled major risk factors
6. Elevated Lp(a)
7. Chronic Kidney Disease (CKD)

Comorbidities defined as DM, recent acute ASCVD event, ASCVD event while on statin, baseline LDL-C ≥190 mg/dl, uncontrolled major

Writing Committee et al. *J Am Coll Cardiol*. 2016; 68:92–125.

See enlargement, p. 31

Stable Clinical ASCVD Without Comorbidities



Writing Committee et al. *J Am Coll Cardiol*. 2016; 68:92–125.

See enlargement, p. 32

Stable Clinical ASCVD Without Comorbidities

- On maximally tolerated statin
- Threshold for considering non-statin
  - ≥50% LDL-C reduction
  - (May consider LDL-C <100 mg/dL)
- Consider 1st: Ezetimibe (may consider BAS if ezetimibe intolerant + TG <300 mg/dL)
- Consider 2nd: PCSK9 inhibitor in addition or as replacement for ezetimibe

Writing Committee et al. *J Am Coll Cardiol.* 2016; 68:92–125.

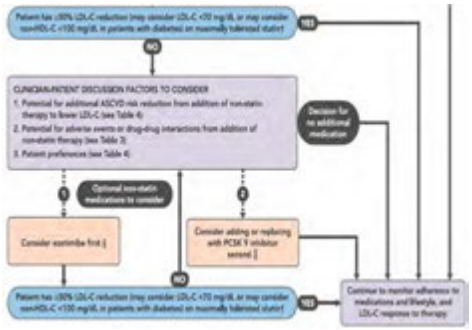
Case 2

- 59-year old woman admitted for acute MI
- PMH: hypercholesterolemia, chronic stable angina
- States adherence to atorvastatin 80 mg/day (and other meds) + lifestyle modifications
- LDL-C has ↓ 51% from baseline
- LDL-C 90 mg/dL

Which of the following do you recommend?

A. Pt has achieved acceptable LDL-C reduction. No modifications to therapy are needed.
B. Pt should receive moderate-intensity statin + ezetimibe.
C. Pt should receive statin + niacin extended-release.
D. Clinician and pt should consider potential net ASCVD risk-reduction benefit of adding non-statin & pt preferences.

Clinical ASCVD with Comorbidities



Writing Committee et al. *J Am Coll Cardiol*. 2016; 68:92–125.

See enlargement, p. 32

Clinical ASCVD with Comorbidities

- On maximally tolerated statin
- Threshold for considering non-statin
  - ≥50% LDL-C reduction
  - (May consider LDL-C <70 mg/dL or non-HDL-C <100 mg/dL in pts with diabetes)
- Consider 1st: Ezetimibe (may consider BAS if ezetimibe intolerant + TG <300 mg/dL)
- Consider 2nd: PCSK9 inhibitor in addition or as replacement for ezetimibe

Writing Committee et al. *J Am Coll Cardiol*. 2016; 68:92–125.

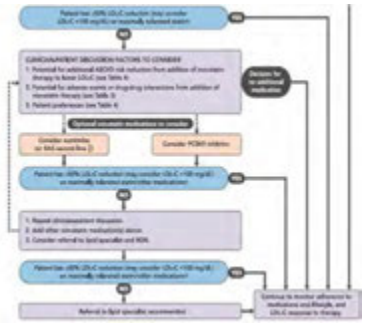
Case 3

- 38-year old man presents for follow-up in the clinic
- PMH: hypercholesterolemia, HTN
- FH: premature ASCVD events
- States adherence to rosuvastatin 40 mg/day + lifestyle modifications
- Recently lost 10 pounds with lifestyle modifications
- LDL-C: Baseline 284 mg/dL, currently 141 mg/dL
- During the clinician-pt discussion, pt says he wants additional therapy to lower his risk of ASCVD events

Which of the following do you recommend?

A. Add colesevelam.
B. Add ezetimibe or a PCSK9 inhibitor.
C. Add lomitapide.
D. Add phytosterols.

Baseline LDL-C ≥190 mg/dL (no Clinical ASCVD)

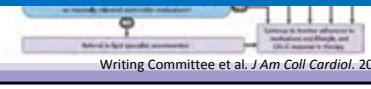


Writing Committee et al. *J Am Coll Cardiol*. 2016; 68:92–125.

See enlargement, p. 33

Baseline LDL-C ≥190 mg/dL (no Clinical ASCVD)

- Same initial clinical steps
- Threshold for considering non-statin
  - ≥50% LDL-C reduction
  - (May consider LDL-C <100 mg/dL)
- Either ezetimibe OR PCSK9 inhibitor
- Referral to lipid specialist recommended (may consider mipomersen, lomitapide, LDL apheresis in appropriate pts)



Writing Committee et al. *J Am Coll Cardiol*. 2016; 68:92–125.

Case 4

- 62-year old woman presents for follow-up in the clinic
- PMH: diabetes, HTN
- States adherence to atorvastatin 40 mg/day + lifestyle modifications
- LDL-C: Baseline 174 mg/dL, currently 108 mg/dL (↓ 38%)
- Non-HDL-C: Currently 153 mg/dL
- 10-yr ASCVD risk > 7.5%
- The pt is willing to take additional medication to lower ASCVD risk.

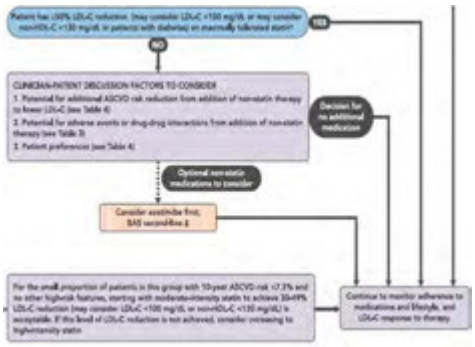
Which of the following thresholds should the addition of non-statin therapy be considered?

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.

Which of the following do you recommend?

A. Pt has achieved anticipated response to high-intensity statin & no other interventions are needed.
B. Increase atorvastatin to 80 mg/day to achieve >50% LDL-C reduction.
C. Clinician-pt discussion should consider potential net ASCVD risk-reduction benefit of adding non-statin & pt preferences.
D. Preferentially consider colesevelam to lower LDL-C & A1C.

Ages 40-75 (no Clinical ASCVD) + Diabetes



Writing Committee et al. *J Am Coll Cardiol*. 2016; 68:92–125.

See enlargement, p. 33

Ages 40-75 (no Clinical ASCVD) + Diabetes

- Same initial clinical steps
- On moderate- or high-intensity statin
- Increase to high-intensity statin if needed
- Threshold for considering non-statin
  - Expected % LDL-C reduction
  - (May consider LDL-C <100 mg/dL or non-HDL-C <130 mg/dL)
- Consider ezetimibe (may consider BAS if ezetimibe intolerant + TG <300 mg/dL)
- PCSK9 inhibitor is not indicated

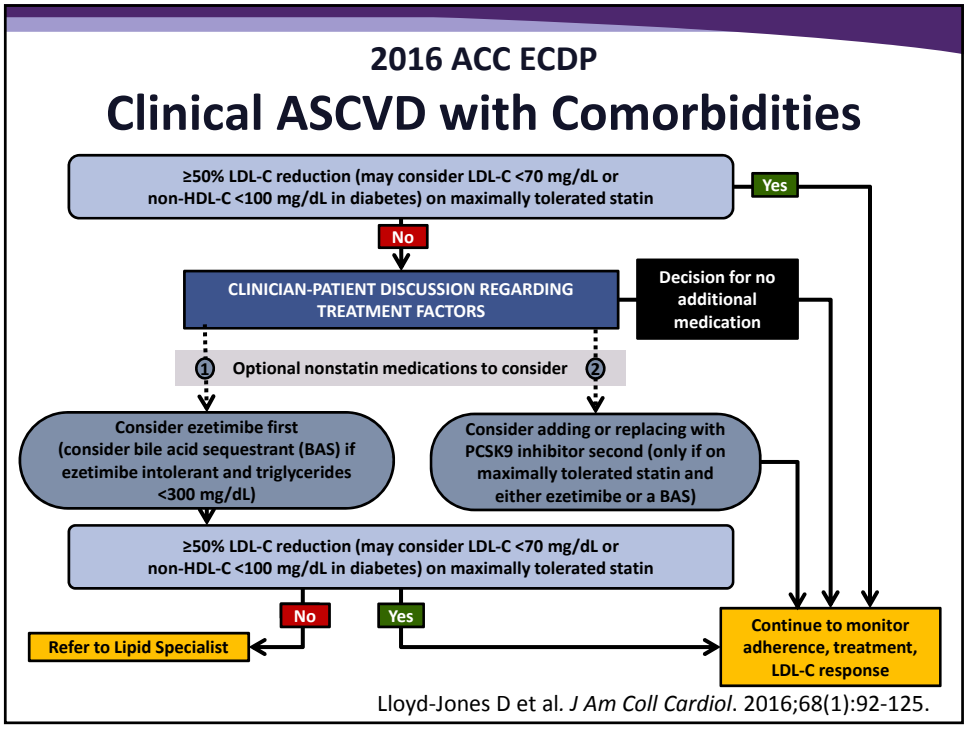
Writing Committee et al. *J Am Coll Cardiol*. 2016; 68:92–125.

Key Takeaways

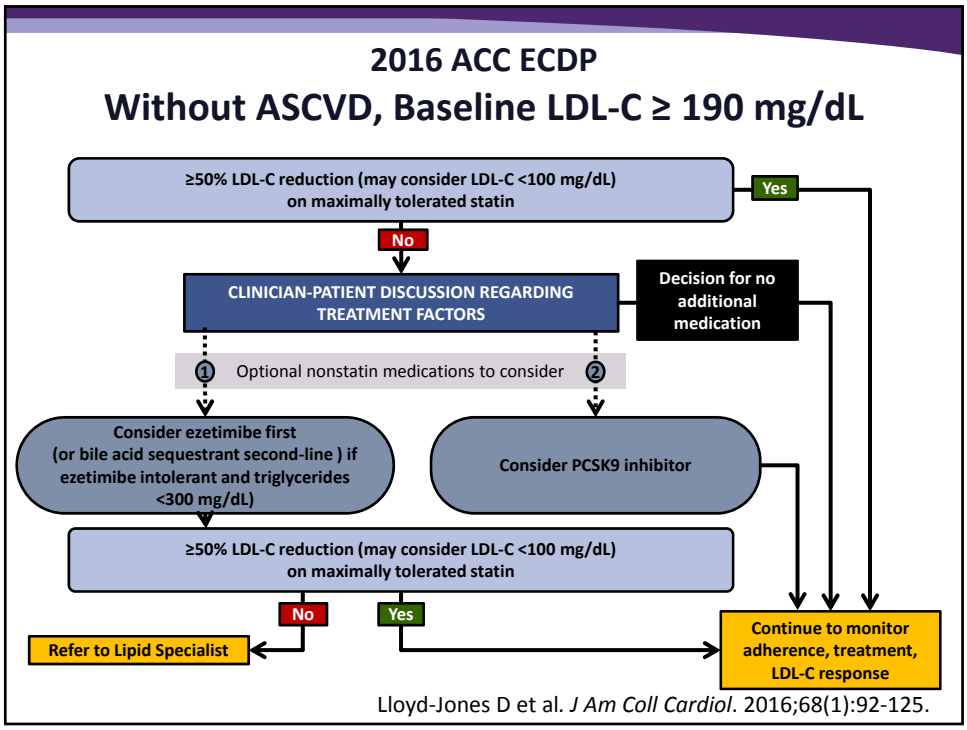
- Statins are the preferred therapy to reduce LDL-C and ASCVD risk
- After maximizing statin therapy, non-statin therapy may be considered for certain high-risk patients who are on maximally tolerated statin therapy and do not achieve adequate LDL-C reduction
- When a non-statin agent is needed, preference should be given to agents that reduce ASCVD risk
- Pharmacists should work with other clinicians to optimize the treatment of patients with hypercholesterolemia

Which of these changes in your practice are you likely to make after today's presentation?

- Read current guideline and expert consensus decision pathway for the treatment of hypercholesterolemia in adults.
- Differentiate the mechanism of action of non-statins with statins for the treatment of hypercholesterolemia.
- Compare your organization's hypercholesterolemia treatment protocols with current guideline and decision pathway.
- Discuss with colleagues the potential role of the non-statin drug therapies in managing patients with hypercholesterolemia in your practice setting.
- Devise a plan for treating patients with hypercholesterolemia who require non-statin therapy.
- Demonstrate to colleagues the role of the pharmacist in managing patients with hypercholesterolemia in your setting.

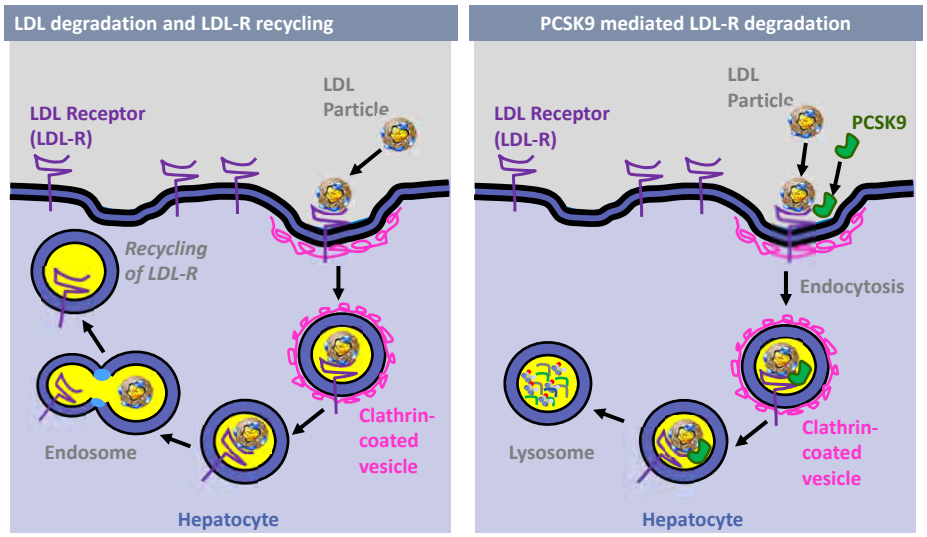


Lloyd-Jones D et al. *J Am Coll Cardiol*. 2016;68(1):92-125.



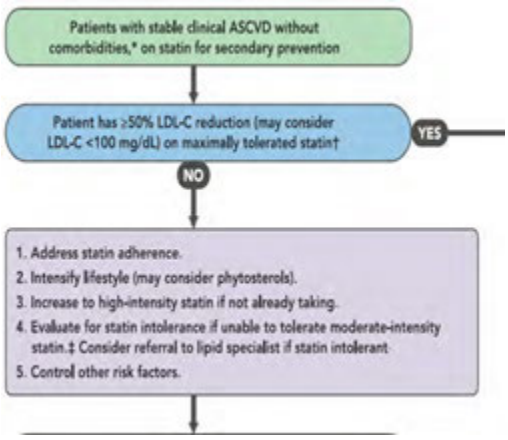
Lloyd-Jones D et al. *J Am Coll Cardiol*. 2016;68(1):92-125.

Proprotein Convertase Subtilisin/Kexin type 9 (PCSK9) Inhibitors



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

Patients with Stable Clinical ASCVD Without Comorbidities



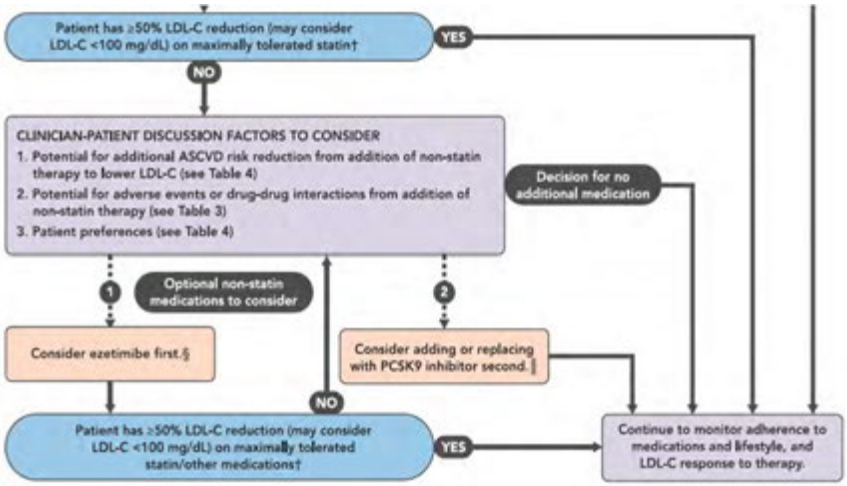
Comorbidities

1. Diabetes mellitus
2. Recent (<3 mo) acute ASCVD event
3. ASCVD event while on statin
4. Baseline LDL-C ≥190 mg/dL
5. Uncontrolled major risk factors
6. Elevated Lp(a)
7. Chronic Kidney Disease (CKD)

Comorbidities defined as DM, recent acute ASCVD event, ASCVD event while on statin, baseline LDL-C ≥190 mg/dl, uncontrolled major

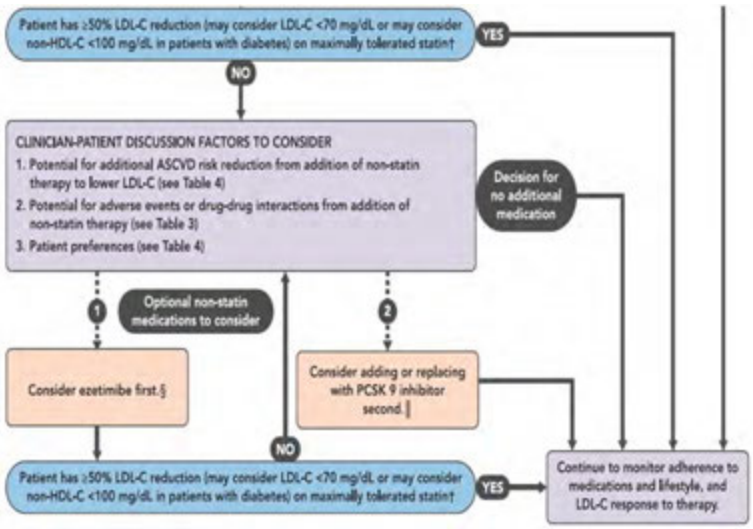
Writing Committee et al. *J Am Coll Cardiol*. 2016; 68:92–125.

Stable Clinical ASCVD Without Comorbidities



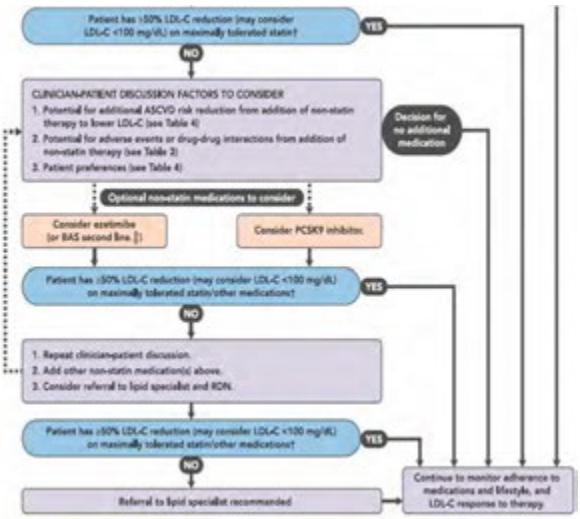
Writing Committee et al. *J Am Coll Cardiol*. 2016; 68:92–125.

Clinical ASCVD with Comorbidities



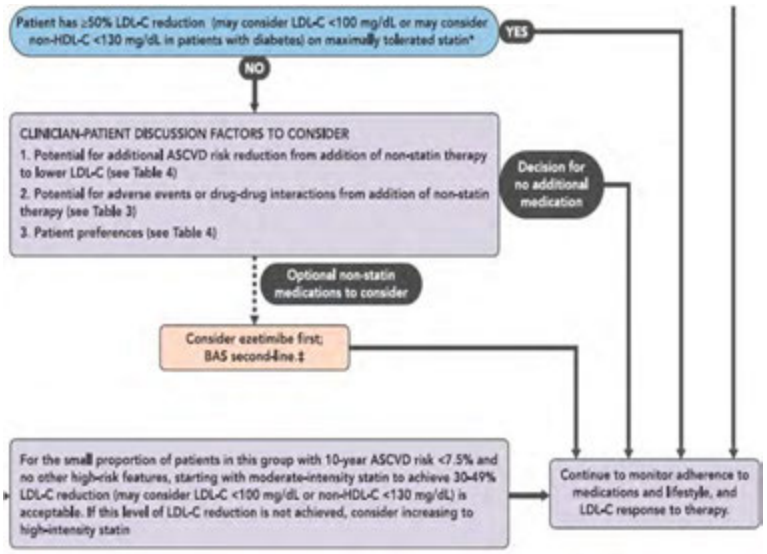
Writing Committee et al. *J Am Coll Cardiol*. 2016; 68:92–125.

Baseline LDL-C ≥190 mg/dL (no Clinical ASCVD)



Writing Committee et al. *J Am Coll Cardiol*. 2016; 68:92–125.

Ages 40-75 (no Clinical ASCVD) + Diabetes



Writing Committee et al. *J Am Coll Cardiol*. 2016; 68:92–125.

Self-Assessment – Case Scenarios

Case 1: A 49-year old man presents for follow-up in the clinic:

- PMH: hypercholesterolemia, chronic stable angina
- States adherence to atorvastatin 20 mg/day (and other meds) + lifestyle modifications
- BMI 32 kg/m2 (stable for 3 years)
- LDL-C has ↓ 42% from baseline
- LDL-C = 130 mg/dL

1. Which of the following do you recommend?

   a. Pt is intolerant to statin therapy. Stop atorvastatin.
   b. Pt had less-than-anticipated response on moderate-intensity statin. Start ezetimibe.
   c. Pt had anticipated response to moderate-intensity statin. Try alternate high-intensity statin therapy prior to adding non-statin.
   d. Clinician and pt should consider potential net ASCVD risk-reduction benefit of adding non-statin & pt preferences.

Case 2: A 59-year old woman admitted for acute MI:

- PMH: hypercholesterolemia, chronic stable angina
- States adherence to atorvastatin 80 mg/day (and other meds) + lifestyle modifications
- LDL-C has ↓ 51% from baseline
- LDL-C 90 mg/dL

2. Which of the following do you recommend?

   a. Pt has achieved acceptable LDL-C reduction. No modifications to therapy are needed.
   b. Pt should receive moderate-intensity statin + ezetimibe.
   c. Pt should receive statin + niacin extended-release.
   d. Clinician and pt should consider potential net ASCVD risk-reduction benefit of adding non-statin & pt preferences.

Case 3: A 38-year old man presents for follow-up in the clinic:

- PMH: hypercholesterolemia, HTN
- FH: premature ASCVD events
- States adherence to rosuvastatin 40 mg/day + lifestyle modifications
- Recently lost 10 pounds with lifestyle modifications
- LDL-C: Baseline 284 mg/dL, currently 141 mg/dL
- During the clinician-pt discussion, pt says he wants additional therapy to lower his risk of ASCVD events

3. Which of the following do you recommend?

    a. Add colesevelam.
    b. Add ezetimibe or a PCSK9 inhibitor.
    c. Add lomitapide.
    d. Add phytosterols.

Case 4: A 62-year old woman presents for follow-up in the clinic:

- PMH: diabetes, HTN
- States adherence to atorvastatin 40 mg/day + lifestyle modifications
- LDL-C: Baseline 174 mg/dL, currently 108 mg/dL (↓ 38%)
- Non-HDL-C: Currently 153 mg/dL
- 10-yr ASCVD risk > 7.5%
- The pt is willing to take additional medication to lower ASCVD risk.

4. Which of the following thresholds should the addition of non-statin therapy be considered?

    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.

5. Which of the following do you recommend?

    a. Pt has achieved anticipated response to high-intensity statin & no other interventions are needed.
    b. Increase atorvastatin to 80 mg/day to achieve >50% LDL-C reduction.
    c. Clinician-pt discussion should consider potential net ASCVD risk-reduction benefit of adding non-statin & pt preferences.
    d. Preferentially consider colesevelam to lower LDL-C & A1C.

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3. Complete all required elements. Go to step six above.

Activity Date:	Tuesday, December 6, 2016	**Code:**		**CE Hours:**	1.5

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