



## BRINGING CLINICIANS TOGETHER TO DISCUSS CURRENT DRUG THERAPY

May 2017  
Vol. 14, No. 5

Based on

The following succinct analysis appeared in *Pharmacist's Letter*.

trc | pharmacist's letter™

Vol. 33, No. 5

### CHOLESTEROL

You'll hear buzz about using the PCSK9 inhibitors, *Repatha* (evolocumab) or *Praluent* (alirocumab), in patients with CV disease.

These injectable meds lower LDL cholesterol by about 60%...but we've been waiting to see if they improve CV outcomes.

Now evidence suggests that adding *Repatha* to a statin in patients with CV disease and other risks (diabetes, etc) prevents one more CV event for every 74 patients treated for about 2 years.

In contrast, ezetimibe (*Zetia*, etc) lowers LDL by about 18%...and prevents one CV event for every 50 acute coronary syndrome patients over about 7 years.

These are the only non-statins with evidence of improved CV outcomes when added to a statin...but they haven't been shown to reduce mortality.

PCSK9 inhibitors cost about \$14,000/yr...ezetimibe \$2,800/yr.

Don't rush to suggest adding either of these meds to a statin.

Instead, continue to emphasize lifestyle changes and adherence to a statin...this also impacts Star Ratings. If muscle symptoms are an issue, look for interacting meds...or consider a short-term "statin holiday."

Recommend ezetimibe first for patients who need a statin add-on... such as those with CV disease who can't tolerate a high-intensity statin or don't get the expected LDL-lowering from their statin.

For now, advise saving PCSK9 inhibitors for those with VERY high LDL due to familial hypercholesterolemia...or for patients at highest CV risk.

For example, a PCSK9 inhibitor may be tried if a patient has a CV event on a high-intensity statin and ezetimibe...or has CV disease and multiple risks such as hypertension, diabetes, and smoking.

But expect payers to continue to require prior auths to limit PCSK9 inhibitor use...and don't expect a big uptick in these specialty Rx's.

Explain that concerns about very low LDL...such as below 25 mg/dL... aren't showing up in short-term studies. So far there doesn't seem to be a link with cataracts or adverse musculoskeletal or neurologic effects.

Expect CV outcome data with *Praluent* in the next year or two.

Listen to *PL VOICES* for a fascinating discussion with a guideline author about the role of PCSK9 inhibitors. And see our *Lipid Treatment FAQs* chart for useful management strategies.

(For more on this topic, see Clinical Resource #330510 at [PharmacistsLetter.com](http://PharmacistsLetter.com).)

Primary Reference – Sabatine MS, Giugliano RP, Keech AC, et al. Evolocumab and clinical outcomes in patients with cardiovascular disease. *N Engl J Med* Published online Mar 17, 2017; doi:10.1056/NEJMoa1615664.

See LEADER NOTES for answers to discussion questions

Discussion Questions

**Overview of current therapy**

1. What is known about the cardiovascular benefits of statins and non-statins?

**Analysis of new study**

2. What type of study was this? How were the patients selected for inclusion?

3. How were the study groups defined?

4. How were the outcomes evaluated?

**5. What were the outcomes of this study?**

**6. What were the strengths and weaknesses of this study?**

**7. Were the results expressed in terms we care about and can use?**

**How should the new findings change current therapy?**

**8. Do the results change your practice? How?**

**Apply the new findings to the following case**

K.H. is a 63-year-old female who is well known to you. She has COPD due to a 20-pack-year smoking history, and is currently well-controlled with tiotropium 18 mcg daily. She recently underwent a triple cardiac bypass for coronary artery disease (CAD). While in the hospital, her LDL was found to be 220 mg/dL. She was prescribed two weeks of atorvastatin 80 mg, along with lisinopril 5 mg daily, metoprolol XL 25 mg daily, and aspirin 81 mg daily, and was advised to follow up with her primary care provider for further management. K.H. presents to the clinic today for her first follow-up visit complaining of muscle aches that she is attributing to her new statin prescription.

**9. How might you address K.H.'s concerns about statin-related muscle aches?**

You check K.H.'s CK, vitamin D, and thyroid level. The results are normal. You decrease her atorvastatin dose to 20 mg daily and advise her to gradually increase back up to 80 mg daily as tolerated.

**10. Is monitoring K.H.'s LDL necessary? How much of an LDL decrease should you expect?**

K.H.'s LDL returns at 195 mg/dL after 8 weeks of atorvastatin 80 mg daily.

**11. What are the options for managing K.H.'s LDL?**

K.H. admits she hasn't actually been taking her medication because she saw a commercial stating statins could cause diabetes and wonders if the risks might outweigh the benefits for her.

**12. How should you address K.H.'s concern?**

K.H. appreciates that you take the time to help her weigh the benefits and risks of statin treatment. She decides to start taking her atorvastatin 80 mg daily. K.H.'s repeat LDL level in 6 weeks is 95 mg/dL and she denies any muscle-related symptoms.

See LEADER NOTES for answers to discussion questions

## References

Bohula EA, Morrow DA, Giugliano RP, et al. Atherothrombotic risk stratification and ezetimibe for secondary prevention. *J Am Coll Cardiol* 2017;69(8):911-21.

Cannon CP, Blazing MA, Giugliano RP, et al. Ezetimibe added to statin therapy after coronary syndromes. *N Engl J Med* 2015;372(25):2387-97.

Lloyd-Jones DM, Morris PB, Ballantyne CM, et al. 2016 ACC expert consensus decision pathway on the role of non-statin therapies for LDL-cholesterol lowering in the management of atherosclerotic cardiovascular disease risk: a report of the American College of Cardiology Task Force on Clinical Expert Consensus Documents. *J Am Coll Cardiol* 2016;68(1):92-125.

Robinson JG, Huijgen R, Ray K, et al. Determining when to add nonstatin therapy: a quantitative approach. *J Am Coll Cardiol* 2016;68(22):2412-21.

Robinson JG, Rosenson RS, Farnier M, et al. Safety of very low low-density lipoprotein cholesterol levels with alirocumab: pooled data from randomized trials. *J Am Coll Cardiol* 2017; 69(5):471-82.

Sabatine MS, Giugliano RP, Keech AC, et al. Evolocumab and clinical outcomes in patients with cardiovascular disease. *N Engl J Med* Published online Mar 17, 2017; doi:10.1056/NEJMoa1615664.

Sattar N, Preiss D, Murray HM, et al. Statins and risk of incident diabetes: a collaborative meta-analysis of randomised statin trials. *Lancet* 2010;375(9716):735-42.

Schwartz GG, Bessac L, Berdan LG, et al. Effect of alirocumab, a monoclonal antibody to PCSK9, on long-term cardiovascular outcomes following acute coronary syndromes: rationale and design of the ODYSSEY outcomes trial. *Am Heart J* 2014;168(5):682-9.

Stone NJ, Robinson JG, Lichtenstein AH, et al. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation* 2014;129(25 Suppl 2):S1-45.

### **Additional Pharmacist's Letter Resources** available at [PharmacistsLetter.com](http://PharmacistsLetter.com)

Chart, Lipid Treatment FAQs. *Pharmacist's Letter/Prescriber's Letter*. May 2017.

Chart, Non-Statins Lipid-Lowering Agents. *Pharmacist's Letter/Prescriber's Letter*. May 2017.

PL VOICES, Monitoring LDL in Patients on a Statin. *Pharmacist's Letter/Prescriber's Letter*. March 2017.

PL VOICES, Statins in Patients with Diabetes. *Pharmacist's Letter/Prescriber's Letter*. December 2016.

Chart, Statin Dose Comparison. *Pharmacist's Letter/Prescriber's Letter*. June 2016.

Chart, Clinically Significant Statin Drug Interactions. *Pharmacist's Letter/Prescriber's Letter*. March 2016.

PL VOICES, Role of Statins and Blood Pressure Medications in Primary Prevention of CV Disease. *Pharmacist's Letter/Prescriber's Letter*. May 2016.

Commentary, BP and Lipid-Lowering Therapy in Primary Prevention: HOPE-3. *Pharmacist's Letter/Prescriber's Letter*. May 2016.

Chart, *Repatha* and *Praluent* Comparison. *Pharmacist's Letter/Prescriber's Letter*. October 2015.

PL VOICES, Managing Statin Intolerance. *Pharmacist's Letter/Prescriber's Letter*. September 2015.

Chart, Statin Muscle Symptoms: Managing Statin Intolerance. *Pharmacist's Letter/Prescriber's Letter*. September 2015.

PL VOICES, Non-Statins for Dyslipidemia. *Pharmacist's Letter/Prescriber's Letter*. July 2015.

PL VOICES, Safety and Efficacy of Niacin. *Pharmacist's Letter/Prescriber's Letter*. September 2014.

PL VOICES, The Current Cholesterol Controversy. *Pharmacist's Letter/Prescriber's Letter*. July 2014.

Chart, 2013 ACC/AHA Cholesterol Guidelines. *Pharmacist's Letter/Prescriber's Letter*. January 2014.

Chart, Characteristics of the Various Statins. *Pharmacist's Letter/Prescriber's Letter*. December 2013.

## Welcome to PL Journal Club

PL Journal Club gives you insights and guides you to the discoveries that *Pharmacist's Letter* researchers and editors uncover. Each month we analyze many new studies and help you discover the answers to the hard questions. "What are the real advantages and disadvantages of new therapies?" "How do they compare with other options?" "What do pharmacists and prescribers need to know?" We look beyond the headlines and promotional materials to interpret the clinical studies and data. Sometimes the marketing spin doesn't stand up to scrutiny. Sometimes studies do not really prove what they are reported to prove. PL Journal Club helps guide you to the truth and how to apply new findings to patient care.

PL Journal Club builds on *Pharmacist's Letter* to provide you with background for your own journal club discussions. We won't bring up every possible question, but you can...in your own group meetings. If a question comes up, go to [PharmacistsLetter.com](http://PharmacistsLetter.com) to find more background. As a PL Journal Club participant, you get access to all of *Pharmacist's Letter*. Feel free to call or email us with suggestions or if we can be of assistance... 209-472-2240 or [PLJournalClub@pletter.com](mailto:PLJournalClub@pletter.com).

## Instructions

Go to [PharmacistsLetter.com](http://PharmacistsLetter.com) to get the PL Journal Club PARTICIPANT NOTES. Use the search function to look for "Journal Club." You'll also get great background materials, including *Pharmacist's Letter* and clinical resources. PL Journal Club functions like a typical group meeting, except that it is organized for you with the expert analysis of important new studies done by the large *Pharmacist's Letter* research and editorial staff. Let the questions serve as a springboard for your discussions. Use our patient cases or your own cases to shape the discussion. Each month, PL Journal Club reviews a topic that is also covered in *Pharmacist's Letter*. You'll also find a library of previous PL Journal Clubs online for your use.

## PL Journal Club Contributing Editors:

Lori Dickerson, PharmD, FCCP, *Editor*; Jennifer Nieman, PharmD, BCPS, *Assistant Editor*; Lisa D. Mims, MD, Department of Family Medicine, Medical Univ of South Carolina, Charleston, SC; Maribeth Porter, MD, Department of Community Health and Family Medicine, Univ of Florida, Gainesville, FL.

**Editors and Authors:** Jeff Jellin, PharmD, *Editor-in-Chief*; Sherri Boehringer, PharmD, BCPS, *Senior Editor, VP Content*; Karen Davidson, PharmD, *Senior Editor*; Tammie Armeni, RPh, PharmD, *Editor, Director of Continuing Education*; Melissa Blair, PharmD, FASHP, FCCP, BCPS; Sandye Chabot, PharmD; Lori Dickerson, PharmD, FCCP; Rachel Maynard, PharmD; Kimberly Palacios, PharmD, *Editors*; Stacy Hester, RPh, BCPS; Tanveer Khan, PharmD; Crystal Maric, BSc Pharm, MBA, ACPR, *Associate Editors*; Bethany Bryant, PharmD, BCPS; Vickie Danaher, PharmD; Flora Harp, PharmD; Tanner Higginbotham, PharmD; Jennifer Nieman, PharmD, BCPS; Brea Rowan, PharmD, BCPS; James Van, BSc Pharm; Don Weinberger, PharmD; Marlea Wellein, PharmD, BCPS, *Assistant Editors*; Karen Wilson, BA, *Manuscript Editor*; Minda Paglinawan, BA, *Assistant Manuscript Editor*; Jenni Mangrum, BS, CPhT, *Assistant Education and Accreditation Editor*; Mark Graber, MD, MSHCE, FACEP, *Associate Clinical Editor*. **Consultants:** Jill Allen, PharmD, BCPS; Melanie Cupp, PharmD, BCPS; Katie Lacaria, BSc Pharm, ACPR; Heidi Liston, BSc Pharm, PharmD; Lu-Ann Murdoch, BSc Pharm; Annette Murray, BSc Pharm; Neeta O'Mara, PharmD, BCPS; Jennifer Pennington, RN, BSN. **Editorial Advisors:** Christophe Anslinger, PA-C; Thomas Barringer, MD, FAHA, FNLA; Christopher Barry, PA-C, MMSc; William Bednar, MD; Larissa Bossaer, PharmD, BCPS; Robert Browne, MD, FFAFP; Stephen Brunton, MD; Holley Bush, PharmD; Peter Carek, MD, MS; Gary Choy, PharmD; Matthew Cline, MD; John Connolly, MD, FACP, FCCP; Sandra Counts, PharmD; Hikmat Fikrat, PhD; Rex Force, PharmD, FCCP, BCPS; Lawrence Frank, MD, FACP; Peter Garbeff, MD; Mark Garofoli, PharmD, MBA, CGP; Charles Green, RPh; Susan Halasi, MSc Pharm; John Hambright, PharmD; Roland Hart, MD; Kyle Herbold, MD; Patricia Hatton, MD; Sydney Hendry, MD; Raissa Hill, DO; Jerry Jones, MD; Sheela Kapre, MD, FACP, FCCP; Adam Kaye, PharmD, FASCP, FCPhA; William Kehoe, PharmD, MA, FCCP, BCPS; Joshua Lenchus, DO, RPh, FACP, SFHM; Stanley Leong, PharmD; Kevin Maeda, PharmD; Christine Marsh, RPh; Eric Matheson, MD, MS; Christina McLaughlin, CPhT, EMT; Kay Niegel, RPh; Mike Pastrick, RPh; Ernest Pieper, PharmD; Daren Primack, MD, FACC; Barbara Rankin, MD; Jenna Reel, PharmD, BCPS, CPP, CDE; George Rishwain, MD; Sandy Robertson, PharmD; Edward Rogan, PharmD, BCACP; Gerald Rubley, MSN, PharmD; Ruth Ruffe, PharmD; AnnieMarie Santos, MD; David Schneider, MD; Allen Shaughnessy, PharmD, MMedEd; Jonathan Szkotak, PharmD, BCACP; Joshua Tessier, DO; Bruce Uch, PharmD; John David Williamson, MD, FFAFP; Raymond Wong, MD; William Yee, PharmD, FASHP, FCSHP; Kent Yep, RPh.

**Advisory Board:** Evan Ballard, MD, Jonesville Family Medical Ctr; Melvin Baron, PharmD, MPA, Univ of Southern Calif; Jan Basile, MD, FACP, Medical Univ of South Carolina; Robert Bickerton, MD, FACP; Reid B. Blackwelder, MD, FFAFP, East Tennessee State Univ; Kevin Brown, MD, FACOG, Texas A&M; R. Keith Campbell, RPh, FFADE, FASHP, FAPhA, CDE, Washington State Univ; Andrea Darby-Stewart, MD, HonorHealth; Anthony A. Donato, Jr., MD, MHPE, Reading Health System; Jan Drutz, MD, Baylor College of Med; Margaret A. Fitzgerald, DNP, FNP-BC, NP-C, FAANP, CSP, FAAN, DCC, Fitzgerald Health Ed Associates; Barry Gidal, PharmD, RPh, Univ of Wisc; Martin Grajower, MD, FACP, FACE, Albert Einstein College of Med; B. Joseph Guglielmo, PharmD, UC San Francisco; Stuart Haines, PharmD, BCPS, BCACP, BC-ADM, FCCP, FASHP, FAPhA, Univ of Miss; Jefferson Harman, Jr, MD, Col, USAF, MC, FS; B. Mark Hess, MD, FACP; John Holman, MD, MPH, FFAFP; Eric Jackson, PharmD, FCCP, BCPS, Univ of Conn; Peter Jacobsen, PhD, DDS, Univ of the Pacific; Paul Jensen, MD, PharmD, FFAFP; Alan David Kaye, MD, PhD, DABA, DABPM, DABIPP, Louisiana State Univ; Steve Kayser, PharmD, UC San Francisco; Brian Kessler, DO, FCOFP, Lincoln-Memorial Univ; Edgar Lerma, MD, FACP, FASN, FAHA, Univ of Illinois at Chicago; Evan L. Lipkis, MD; Mark McConnell, MD, Oscar G. Johnson VA Medical Ctr; Stephen L. McKernan, BSc Pharm, ND, DO, FFAFP, Sam Houston State Univ; Steven E. Nissen, MD, MACC, Cleveland Clinic; Brenden O'Hara, RPh, BCACP, Blue Cross/Blue Shield of NC; Douglas S. Paauw, MD, MACP, Univ of Washington; Dan Perri, BSc Pharm, MD, FRCPC, McMaster Univ; Charles Ponte, BS, PharmD, FFADE, FAPhA, FASHP, FCCP, FNAP, West Virginia Schools of Pharmacy & Medicine; Joseph E. Scherger, MD, MPH, Eisenhower Medical Ctr; Arthur Shinn, PharmD, FASCP, Managed Pharmacy Consultants; Kelly Anne Spratt, DO, FACC, Univ of Pennsylvania; Dan Steiber, RPh, Genesis Pharma Consultants; Tom Vickery, PharmD, OPTION Care; C. Wayne Weart, PharmD, FAPhA, FASHP, BCPS, Medical Univ of South Carolina; Craig D. Williams, PharmD, FNLA, BCPS, Oregon Health & Science Univ.

## DISCLOSURE:

The editors of this activity and its publisher, Therapeutic Research Center, have no relevant financial interests related to the products or services covered by this activity. Therapeutic Research Center/*Pharmacist's Letter* does not receive any commercial support and does not accept any advertising. It is completely independent and is supported entirely by subscriptions. *Pharmacist's Letter* focuses on delivering completely objective, unbiased drug information and advice for the benefit of subscribers.

Unbiased Evidence and Recommendations for the Pharmacist  
on New Developments in Drug Therapy



| pharmacist's letter journal club™

3120 West March Lane, Stockton, CA 95219  
TEL (209) 472-2240 ~ FAX (209) 472-2249



| pharmacist's letter™

[PharmacistsLetter.com](http://PharmacistsLetter.com)

The contents are copyrighted. © 2017 Therapeutic Research Center. All Rights Reserved.