



BRINGING CLINICIANS TOGETHER TO DISCUSS CURRENT DRUG THERAPY

 August 2017
 Vol. 14, No. 8

Based on

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


 pharmacist's letter™

Vol. 33, No. 8

DIABETES MEDS

You'll hear more controversy about when to use SGLT2 inhibitors (Jardiance, etc) for type 2 diabetes...as more data on CV impact emerge.

Invokana (canagliflozin) joins *Jardiance* (empagliflozin) as a flozin that lowers CV risk when added to metformin in type 2s at high CV risk.

Adding *Invokana* prevents a CV event in one in 333 type 2 patients at very high CV risk over 3.5 years...but doesn't seem to reduce mortality.

But *Jardiance* seems to have an edge. It prevents CV death in one in 45 type 2s with heart disease over 3 years...reduces mortality in one in 39...and slows progression of nephropathy in about one in 16.

Expect CV data for *Farxiga* (dapagliflozin) in about 2 years.

But point out flozins cost about \$430/month. And risks are piling up...UTIs, yeast infections, acute kidney injury, rare ketoacidosis, etc.

Plus now we're seeing toe and mid-foot amputations in about one in 77 patients who use *Invokana* for about 3.5 years.

Lean toward *Jardiance* if a flozin is desired as a metformin add-on for type 2s who've had a CV event...or have multiple CV risks.

It's also okay to think about a flozin for patients at lower CV risk. These meds can lower BP and lead to modest weight loss...but it's too soon to say if they provide CV benefits in these patients.

Caution about using flozins in patients at high risk of amputation due to neuropathy, peripheral vascular disease, foot ulcers, etc. And watch for ketoacidosis risk factors...dehydration, severe illness, etc.

Also consider *Victoza* (liraglutide) as a metformin add-on for type 2 patients at high CV risk. It decreases CV death and overall mortality. But it costs about \$750/month and is injected...GI side effects are common...and it may be linked to rare gallbladder disease.

See our chart, *Diabetes Meds and Cardiovascular Impact*, for more details about how these meds stack up.

(For more on this topic, see Clinical Resource #330801 at PharmacistsLetter.com.)

Primary Reference – Neal B, Perkovic, V, Mahaffey KW, et al. Canagliflozin and cardiovascular and renal events in type 2 diabetes. *N Engl J Med* 2017 Jun 12. doi: 10.1056/NEJMoa1611925. [Epub ahead of print].

See LEADER NOTES for answers to discussion questions

Discussion Questions

Overview of current therapy

1. What is known about the cardiovascular (CV) effects of the SGLT2 inhibitors?

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 trial?

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

D.A. is a 57-year-old Latin American male who presents for a physical required by his employer. His past medical history is significant for obesity, hypertension, diabetes, stage 3 chronic kidney disease, and an MI 2 years ago. D.A. is required to have his labs drawn twice a year by his employer, and he has brought his most recent results with him.

His blood pressure is well controlled today at 119/61 mmHg on carvedilol 3.125 mg twice daily and lisinopril 20 mg daily. He is currently taking metformin 1000 mg twice daily for his diabetes and reminds you that he cannot take any insulin due to his profession.

Although D.A. has changed his dietary and exercise habits and has lost 10 pounds over the past 3 months, his A1C is still elevated at 8.7%. His BMP is normal with the exception of a fasting glucose of 195 mg/dL and creatinine of 1.5 mg/dL (estimated glomerular filtration rate \approx 50 mL/min).

See LEADER NOTES for answers to discussion questions

9. Is D.A. receiving appropriate first-line treatment for type 2 diabetes?

D.A. is aware that his A1C is still elevated even though he is eating better, exercising, and taking his medication as prescribed. He has seen commercials for the diabetes medication *Invokana* and was intrigued by the claims of weight loss. He asks if this would be an appropriate medication to add to his regimen.

10. What should you discuss with D.A. about the benefits and risks of the SGLT2 inhibitors?

D.A. appreciates your explanation, and decides he would like to start a trial of *Jardiance* to try to further lower his A1C. He is happy to hear about the potential CV protection that this treatment may provide.

11. What additional measures should you discuss with D.A. to lower his CV risk?

Because D.A. has a history of an MI, you discuss starting a high-intensity statin such as atorvastatin 80 mg daily along with low-dose aspirin for secondary CV prevention.

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Additional Pharmacist's Letter Resources available at PharmacistsLetter.com

- Toolbox, Improving Outcomes After Myocardial Infarction. *Pharmacist's Letter/Prescriber's Letter*. August 2017.
- Chart, Drugs for Type 2 Diabetes. *Pharmacist's Letter/Prescriber's Letter*. July 2017.
- PL Voices, Choosing Metformin Add-Ons. *Pharmacist's Letter/Prescriber's Letter*. February 2017.
- Toolbox, Improving Diabetes Outcomes. *Pharmacist's Letter/Prescriber's Letter*. January 2017.
- Chart, Comparison of GLP-1 Agonists. *Pharmacist's Letter/Prescriber's Letter*. December 2016.
- PL Voices, Treatment of Newly-Diagnosed Type 2 Diabetes. *Pharmacist's Letter/Prescriber's Letter*. October 2016.
- Algorithm, Management of New-Onset Type 2 Diabetes. *Pharmacist's Letter/Prescriber's Letter*. October 2016.
- PL Voices, Cardiovascular Effects of Diabetes Medications. *Pharmacist's Letter/Prescriber's Letter*. August 2016.
- Chart, Diabetes Medications and Cardiovascular Impact. *Pharmacist's Letter/Prescriber's Letter*. August 2016.
- PL Voices, Renal Effects of Diabetes Medications. *Pharmacist's Letter/Prescriber's Letter*. August 2016.
- Chart, Management of Microalbuminuria: Focus on Pharmacotherapy. *Pharmacist's Letter/Prescriber's Letter*. July 2016.
- Commentary, DPP-4 Inhibitors (Gliptins) and Risk of Heart Failure. *Pharmacist's Letter/ Prescribers Letter*. June 2016.
- Commentary, Clinical Use of Metformin in Special Populations. *Pharmacist's Letter/ Prescriber's Letter*. June 2016.
- Chart, Diabetic Foot Infections. *Pharmacist's Letter/Prescriber's Letter*. April 2016.
- PL Voices, Helping Patients Stick with Metformin. *Pharmacist's Letter/ Pharmacist's Letter*. December 2015.
- Algorithm, Improving Tolerability of Metformin. *Pharmacist's Letter/Pharmacist's Letter*. December 2015.
- PL Voices, Cardiovascular Outcomes with Empagliflozin (*Jardiance*). *Pharmacist's Letter/Prescriber's Letter*. November 2015.
- Commentary, Empagliflozin and Cardiovascular Disease. *Pharmacist's Letter/Prescriber's Letter*. November 2015.
- Article, Whether *Invokana* (canagliflozin) and other SGLT2 inhibitors or "flozins" are linked to ketoacidosis. *Pharmacist's Letter/Prescriber's Letter*. July 2015.

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 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.

Instructions

Go to 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.

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



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