

BRINGING CLINICIANS TOGETHER TO DISCUSS CURRENT DRUG THERAPY

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DIABETES

Trulicity (dulaglutide) will be the third GLP-1 agonist to show CV benefits in some patients with type 2 diabetes.

It joins *Ozempic* (semaglutide) and *Victoza* (liraglutide). All three lower CV risk in type 2 patients with CV disease or at high CV risk.

Each of these meds also seems to slow progression to albuminuria... but isn't shown to delay dialysis.

Victoza may still have an edge for now...it's the only GLP-1 agonist shown to reduce CV and overall mortality.

Other GLP-1 agonists...*Adlyxin*, *Bydureon*...are CV neutral.

Continue to advise starting with metformin for type 2 diabetes.

When a GLP-1 agonist is the preferred metformin add-on, generally recommend *Ozempic*, *Trulicity*, or *Victoza*. Most payers cover at least one of these...although co-pays may vary.

Plus there's not a compelling reason to consider other GLP-1 agonists. They don't give more A1C reduction or weight loss...or have fewer GI side effects or injection site reactions. All are costly.

Weigh preferences. For example, lean toward *Victoza* for mortality benefit in a high-CV-risk patient...if they don't mind a daily injection. Or think about *Ozempic* or *Trulicity* for weekly dosing...at a lower cost.

Use the following comparisons to fine-tune your recommendations.

GLP-1 Agonist	CV Effects	~ A1C Decrease	~ Short-Term Weight Loss	~ Injection Site Reactions	~ Cost/Month	Dosing Frequency
Dulaglutide (<i>Trulicity</i>)	↓ Risk	1.5%	6 lb	0.5%	\$760	Once WEEKLY
Liraglutide (<i>Victoza</i>)	↓ Risk	1.5%	6 lb	2%	\$920	Once DAILY
Semaglutide (<i>Ozempic</i>)	↓ Risk	1.5%	9 lb	0.2%	\$770	Once WEEKLY
Exenatide ER (<i>Bydureon</i> , <i>Bydureon BCise</i>)	Neutral	1.5%	3 – 6 lb	17% – 24%	\$700	Once WEEKLY
Lixisenatide (<i>Adlyxin</i>)	Neutral	1%	4 lb	4%	\$620	Once DAILY
Exenatide (<i>Byetta</i>)	No data	1%	4 lb	< 2%	\$730	Twice DAILY

Recommend aiming for doses with CV benefit...*Ozempic* 0.5 mg or 1 mg weekly, *Trulicity* 1.5 mg weekly, or *Victoza* 1.8 mg daily.

Watch for an ORAL semaglutide possibly later this year.

To suggest the most appropriate GLP-1 agonist for your patient, see our in-depth chart, *Comparison of GLP-1 Agonists*. Get our chart, *Diabetes Meds and CV Impact*, for outcomes of SGLT2 inhibitors and other meds.

(For more on this topic, see *Clinical Resource #350807* at PharmacistsLetter.com.)

Primary Reference – Gerstein HC, Colhoun HM, Dagenais GR, et al. Dulaglutide and cardiovascular outcomes in type 2 diabetes (REWIND): a double-blind, randomised placebo-controlled trial. *Lancet* 2019;394:121-30.

See LEADER NOTES for answers to discussion questions.

DISCUSSION QUESTIONS

OVERVIEW OF CURRENT THERAPY

1. What is known about the cardiovascular (CV) effects of glucagon-like peptide-1 (GLP-1) receptor agonists in patients with type 2 diabetes?
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?

See [LEADER NOTES](#) for answers to discussion questions.

6. What were the strengths and weaknesses of this trial?

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

HOW SHOULD THE NEW GUIDELINES CHANGE CURRENT THERAPY?

8. Do the results change your practice? How?

APPLY THE NEW FINDINGS TO THE FOLLOWING CASE

RM is a 57-year-old African American male with a past medical history of obesity, hypertension, type 2 diabetes, MI, and heart failure with reduced ejection fraction (HFrEF) who is in clinic for a routine follow-up. You note that his blood pressure is well controlled today at 119/61 on carvedilol 3.125 mg twice daily and lisinopril 20 mg daily. He is also taking aspirin 81 mg daily and atorvastatin 80 mg daily.

You review RM's lab work and see that his A1C is elevated at 9.2%, despite lifestyle changes over the past 3 months that have led to a 10-pound weight loss.

9. Which medication is first-line for most patients with type 2 diabetes? How should you manage RM?

See [LEADER NOTES](#) for answers to discussion questions.

You start RM on metformin 500 mg daily with a plan to titrate up to 1,000 mg twice daily over the next 4 weeks.

He returns to your office 3 months later for a follow-up visit. He is tolerating the metformin well and has successfully titrated to 1,000 mg twice daily. A recheck of his A1C returns at 8.5%. He knows that this is above his goal and asks for your recommendation for additional medications. He would like to avoid medications associated with further weight gain, as he is already considered obese, and medications that may worsen his heart failure.

10. What metformin add-on options are not preferred for RM??

RM has seen commercials for the diabetes medication *Trulicity* and was intrigued by the claims of weight loss. He asks if this would be an appropriate medication to add to his regimen.

11. What should you consider regarding a GLP-1 agonist as a metformin add-on for RM?

You discuss the benefits and risks of GLP-1 agonists with RM and he would like to start one. Because RM has CV disease, you choose *Trulicity*, since it's shown to reduce CV risk and is covered by his insurance.

12. What adverse effects should you discuss with RM before starting *Trulicity*?

See [LEADER NOTES](#) for answers to discussion questions.

REFERENCES

- American Diabetes Association. 9. Pharmacologic approaches to glycemic treatment: standards of medical care in diabetes-2019. *Diabetes Care* 2019;42(Suppl 1):S90-S102.
- Gerstein HC, Colhoun HM, Dagenais GR, et al. Dulaglutide and cardiovascular outcomes in type 2 diabetes (REWIND): a double-blind, randomised placebo-controlled trial. *Lancet* 2019;394:121-30.
- Gerstein HC, Colhoun HM, Dagenais GR, et al. Dulaglutide and renal outcomes in type 2 diabetes: an exploratory analysis of the REWIND randomised, placebo-controlled trial. *Lancet* 2019;394:131-38.
- Holman RR, Bethel MA, Mentz RJ, et al. Effects of once-weekly exenatide on cardiovascular outcomes in type 2 diabetes. *N Engl J Med* 2017;377:1228-39.
- Husain M, Birkenfeld AL, Donsmark M, et al. Oral semaglutide and cardiovascular outcomes in patients with type 2 diabetes. *N Engl J Med* 2019 Jun 11. doi: 10.1056/NEJMoa1901118. [Epub ahead of print]
- Marso SP, Bain SC, Consoli A, et al. Semaglutide and cardiovascular outcomes in patients with type 2 diabetes. *N Engl J Med* 2016;375:1834-44.
- Marso SP, Daniels GH, Brown-Frandsen K, et al. Liraglutide and cardiovascular outcomes in type 2 diabetes. *N Engl J Med* 2016;375:311-22.
- Neal B, Perkovic V, Mahaffey KW, et al. Canagliflozin and cardiovascular and renal events in type 2 diabetes. *N Engl J Med* 2017;377:644-57.
- Pfeffer MA, Claggett B, Diaz R, et al. Lixisenatide in patients with type 2 diabetes and acute coronary syndrome. *N Engl J Med* 2015;373:2247-57.
- Zinman B, Wanner C, Lachin JM, et al. Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. *N Engl J Med* 2015;373:2117-28.

Additional Pharmacist's Letter Resources available at PharmacistsLetter.com

- Chart, Comparison of GLP-1 Agonists. *Pharmacist's Letter/Prescriber's Letter*. August 2019.
- Chart, Diabetes Medications and Cardiovascular Impact. *Pharmacist's Letter/Prescriber's Letter*. August 2019.
- Chart, Drugs for Type 2 Diabetes. *Pharmacist's Letter/Prescriber's Letter*. July 2019.
- Toolbox, Improving Diabetes Outcomes. *Pharmacist's Letter/Prescriber's Letter*. March 2019.
- Chart, Perioperative Management of Diabetes. *Pharmacist's Letter/Prescriber's Letter*. March 2019.
- Chart, Management of Albuminuria: Focus on Pharmacotherapy. *Pharmacist's Letter/Prescriber's Letter*. September 2018.
- Chart, Combination Therapy with a GLP-1 Agonist. *Pharmacist's Letter/Prescriber's Letter*. July 2018.
- Chart, Continuous Glucose Monitoring FAQs. *Pharmacist's Letter/Prescriber's Letter*. February 2018.
- Chart, Comparison of Blood Glucose Meters. *Pharmacist's Letter/Prescriber's Letter*. February 2018.
- Chart, Comparison of Insulins. *Pharmacist's Letter/Prescriber's Letter*. December 2017.
- Commentary, GLP-1 Agonists and Gallbladder Disease. *Pharmacist's Letter/Prescriber's Letter*. October 2016.

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See **LEADER NOTES** for answers to discussion questions.