

Why does a recent guideline recommend against the use of DPP4 inhibitors such as linagliptin (Trajenta[®]) in people with type 2 diabetes?

Conclusion: The American College of Physicians 2024 guideline advises against adding a DPP4 inhibitor (DPP4i) to metformin because they do not improve patient-important outcomes (morbidity, mortality). DPP4i are relatively costly and people are more likely to benefit from SGLT2 inhibitors (SGLT2i) or GLP1 agonists (GLP1a).

The BC Provincial Academic Detailing (PAD) service continues to deliver the topic <u>T2DM Focused Update: SGLT2</u> <u>Inhibitors & GLP1 Agonists</u>. This topic highlights the evidence of SGLT2i and GLP1a in improving morbidity and mortality in people with type 2 diabetes.

- a) What does the 2024 guideline recommend? The American College of Physicians recommends against adding a DPP4i to metformin in people with type 2 diabetes (strong recommendation).¹ Their systematic review demonstrates with high certainty that DPP4i do not improve cardiovascular or kidney outcomes or survival (refer to table below).² This review replicates findings of other systematic reviews published in 2021 and 2023.^{3,4}
- b) What does linagliptin (Trajenta) cost? The annual drug cost of linagliptin is ~\$940. For comparison, dapagliflozin costs ~\$270 per year, empagliflozin ~\$1090 and semaglutide subcutaneous 1 mg ~\$2960.⁵
- c) Can linagliptin (Trajenta) be used in renal impairment? Based on small pharmacokinetic studies, no dosage adjustment is required in people with renal impairment.⁶ However, linagliptin does not reduce the risk of progression of chronic kidney disease in people with type 2 diabetes.² Further, in a cohort study of older adults, new use of an SGLT2i was associated with a lower risk of acute kidney injury than DPP4i and SGLT2i can be initiated in patients with low eGFRs (20-30 mL/min/1.73²).^{7,8} For more specific information, refer to the December 2022 PAD Refill <u>SGLT2</u> inhibitors in patients with reduced kidney function.
- d) How much does linagliptin (Trajenta) lower HbA1c? When added to metform in people with a baseline HbA1c of approximately 8%, a DPP4i lowers HbA1c by ~0.5%.⁹
- e) Is linagliptin (Trajenta) "insulin sparing"? Compared to placebo, linagliptin reduces the daily insulin requirement by a small amount (1.6 units per day on average) at 1 year.¹⁰ When added to usual care, 3 fewer people out of 100 in the linagliptin group had insulin initiated over 2 years of follow up compared to placebo.¹¹

| DPP4 inhibitors compared with placebo or usual care in people with type 2 diabetes ² | | |
|---|------------------------------|---|
| Death from any cause | RR 1.01 (95%CI 0.94 to 1.08) | no difference; high certainty of evidence |
| Major adverse cardiovascular events | RR 1.00 (95%CI 0.94 to 1.06) | |
| Hospitalization for heart failure | RR 1.06 (95%CI 0.96 to 1.17) | |
| Chronic kidney disease | RR 1.07 (95%CI 0.95 to 1.21) | |

¹QASEEM Ann Intern Med 2024 Apr 29 (PMID:38639546); ²DRAKE Ann Intern Med 2024 Apr 19 (PMID:38639549); ³Cochrane Database Syst Rev 2021;10:CD013650 (PMID: 34693515); ⁴SHI BMJ 2023;381:e074068 (PMID:37024129); ⁵McKesson Pharmaclik; ⁶Health Canada Drug Product Database Trajenta®; ⁷ISKANDER CMAJ 2020;192:E351-60 (PMID:32392523); ⁸BC PAD Service PAD Refill Dec 2022; ⁹TSAPAS Ann Intern Med 2020;173:278-86 (PMID:32598218); ¹⁰YKI-JARVINEN Diabetes Care 2013;12:3875-81 (PMID:24062327); ¹¹CARMELINA JAMA 2019;321:69-79 (PMID:30418475)

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