Can DPP-4 inhibitors be used safely along with metformin in the elderly population?

**Bottom line**

Dipeptidyl peptidase-4 inhibitor (DPPI) plus metformin therapy is generally well tolerated and manageable with a similar adverse event profile and discontinuation rates as metformin alone in older adult patients with type 2 diabetes mellitus (T2DM) (SOR: **B**, systematic review of RCTs). Elderly patients treated with DPPI as add-on therapy compared with patients treated with a conventional oral antidiabetic medication have a significantly lower risk of hypoglycemia (SOR: **B**; prospective cohort study). Treatment of elderly patients with vildagliptin plus metformin is associated with no change in cognitive and functional activity after 1 year of therapy (SOR: **C**; case series).

**Evidence summary**

A systematic review and meta-analysis with significant heterogeneity (19 high-quality RCTs of 3 months’ to 2 year’s duration, N=12,180; mean age 55±10 years; 52% male) evaluated addition of DPPI medications (7 trials sitagliptin, 4 vildagliptin, 3 saxagliptin, 3 linagliptin, and 2 alogliptin) to metformin therapy (DPPI-MET) to evaluate the safety and efficacy of combination therapy versus metformin alone (MET) in patients with T2DM. The safety profile was similar between DPPI-MET and MET groups.

The percentage of patients having at least 1 serious adverse event (AE, “serious” was not defined) was 2.9% in the DPPI-MET group versus 2.7% in the MET group. Discontinuation due to any AE was 2.9% versus 2.1% in the DPPI-MET and MET groups, respectively (no *P* value reported).

A prospective observational study (N=1,188, mean age 71 years, 61% male) compared the effect of add-on therapy of either a DPPI (vildagliptin, sitagliptin, saxagliptin, linagliptin, and alogliptin) or a conventional oral antidiabetic drugs (COAD; eg, sulfonylurea/glinide, thiazolidinedione, or α-glucosidase inhibitor) to current metformin therapy for patients with suboptimally controlled T2DM. Baseline characteristics were similar between the comparison groups for parameters such as duration (years) of T2DM; fasting plasma glucose; hemoglobin A1C measurements; duration of use and dosage of metformin; concomitant treatment with antihypertensive, hypolipidemic agent, or platelet inhibitor; renal function; and percentage of patient with at least 1 diabetic complication.

In the 6-month period after addition of the new medication, fewer patients experienced hypoglycemia with DPPI+MET than with COAD+MET (6% vs 20%; *P*<.001; number needed to treat [NNT]=7) as add-on therapy. Subanalysis showed fewer patients experienced hypoglycemia with DPPI+MET than with a sulfonylurea/glinide (6% vs 26%; *P*<.001; NNT=5). Similarly, fewer patients experienced severe hypoglycemia with DPPI+MET than with COAD+MET (0.1% vs 2.4%; *P*=.001; NNT=43) and with DPPI+MET versus sulfonylurea/glinide (0.1% vs 3.2%; *P*=.001; NNT=32). These authors did not define the criteria for either “hypoglycemia” or “severe hypoglycemia” used in their study.

A case series (N=10, mean age 73 years, 90% female) evaluated the cognitive and functional effects of therapy with vildagliptin 50 mg twice daily plus metformin (1,700–2,000 mg/d) in T2DM. No significant changes for functional or neuropsychological parameters were observed from baseline to follow-up at 6 to 16 months.

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**REFERENCES**


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We invite your questions and feedback. Email us at EBP@fpin.org.