

# Efficacy and safety of dapagliflozin and linagliptin combination in individuals with type 2 diabetes mellitus: A meta-analysis of randomized controlled trials

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## **INTRODUCTION**

- Type 2 diabetes mellitus (T2DM) is a progressive metabolic disorder requiring combination therapy for optimal glycemic control.
- Despite the availability of several oral antidiabetic drugs (OADs), maintaining sustained HbA1c reduction with minimal adverse effects remains challenging.
- Linagliptin (a DPP-4 inhibitor) and dapagliflozin (an SGLT2 inhibitor) act through complementary mechanisms.
- Their combination may provide additive benefits on glycemic control and body weight with an acceptable safety profile.

# **OBJECTIVE**

To evaluate the effect of the dapagliflozin and linagliptin combination compared with other OADs (linagliptin with/or without placebo or dapagliflozin plus vildagliptin) in individuals with T2DM.

### **METHODS**

- PubMed and Google were searched to identify randomized controlled trials (RCTs) evaluating dapagliflozin + linagliptin in adults (≥18 years) with T2DM.
- Studies reporting efficacy and/or safety outcomes of the dapagliflozin + linagliptin combination were included.
- Efficacy Endpoints: Change in HbA1c, fasting plasma glucose (FPG), and postprandial glucose (PPG).
- Safety Endpoints: Change in body weight and incidence of adverse events
- Data were pooled using a random-effects model.
- Meta-analysis was performed with Review Manager (RevMan) version 5.4.
- Sensitivity analyses were conducted to evaluate the robustness of the results.

### **RESULTS** dapagliflozin plus linagliptin other OADs Mean Difference **Mean Difference** Total Mean SD Total Weight IV. Random, 95% CI IV, Random, 95% CI Study or Subgroup Dharmalingam et al. 2024 -1.596 1.08 115 -1.254 1.09 114 -0.34 [-0.62, -0.06] Hong et al. 2025 -1.3 0.5 113 -0.6 0.4 111 32.0% -0.70 [-0.82, -0.58] Jain A, et al. 2024 0.857 108 107 19.7% -0.45 [-0.73, -0.17] -1.28 -0.83 1.229 HbA1c Kumthekar P. et al. 2025 -1.350.64 112 -0.92 0.63 110 28.3% -0.43 [-0.60, -0.26] -0.50 [-0.69, -0.32] 442 100.0% Heterogeneity: $Tau^2 = 0.02$ ; $Chi^2 = 10.54$ , df = 3 (P = 0.01); $I^2 = 72\%$ Test for overall effect: Z = 5.34 (P < 0.00001) Favours dapagliflozin plus linagliptin Favours other OADs dapagliflozin plus linagliptin other OADs Mean Difference Mean Difference SD Total Weight IV, Random, 95% Cl Study or Subgroup Total Mean IV, Random, 95% CI Mean Dharmalingam et al. 2024 -6.13 [-13.90, 1.64] -32.9130 Hong et al. 2025 -50 18 111 25.8% -30.00 [-34.34, -25.66] Jain A. et al. 2024 -26.94 35.96 108 -21.59 42.15 107 23.5% -5.35 [-15.83, 5.13] **FPG** Kumthekar P, et al. 2025 -26.13 13.12 112 -22.59 13.11 110 26.0% -3.54 [-6.99, -0.09] Total (95% CI) 442 100.0% -11.43 [-26.82, 3.96] Heterogeneity: $Tau^2 = 233.97$ ; $Chi^2 = 92.84$ , df = 3 (P < 0.00001); $I^2 = 97\%$ Test for overall effect: Z = 1.46 (P = 0.15) Favours dapagliflozin plus linagliptin Favours other OADs dapagliflozin plus linagliptin Mean Difference Mean Difference other OADs Study or Subgroup SD Total Mean SD Total Weight IV, Random, 95% CI IV, Random, 95% CI 114 28.3% -4.65 [-19.60, 10.30] Dharmalingam et al. 2024 -59.99 59.96 115 -55.34 55.38 Jain A. et al. 2024 -49.16 71.45 108 -29.14 68.94 107 21.7% -20.02 [-38.79, -1.25] **PPG** 112 -30.35 24.76 110 50.0% -21.94 [-28.45, -15.43] Kumthekar P, et al. 2025 -52.29 24.76 335 331 100.0% -16.63 [-27.50, -5.75] Heterogeneity: $Tau^2 = 50.52$ ; $Chi^2 = 4.33$ , df = 2 (P = 0.11); $I^2 = 54\%$ Test for overall effect: Z = 3.00 (P = 0.003) Favours dapagliflozin plus linagliptin Favours other OADs

- **Studies included:** 4 RCTs with 890 participants (1 study: 12 weeks; 3 studies: 16 weeks).
- **HbA1c:** Significant reduction (MD -0.50%; 95% CI -0.69 to -0.32; p<0.001; I<sup>2</sup>=72%). Sensitivity analysis excluding 12-week study: MD -0.42%; I<sup>2</sup>=0%.
- **FPG:** Non-significant reduction (MD –11.43 mg/dL; 95% CI -26.82 to 3.96; p=0.15; I<sup>2</sup>=97%).
- PPG: Significant reduction (MD -16.63 mg/dL; 95% CI -27.50 to -5.75; p=0.003; I<sup>2</sup>=54%).
- **Body weight:** Reduced with combination therapy (MD -0.82 kg; 95% CI -1.02 to -0.61; p<0.001; I<sup>2</sup>=19%).
- **Adverse events**: Comparable between groups (OR 0.80; 95% CI 0.54 to 1.18; p=0.26; I<sup>2</sup>=0%).

# CONCLUSION

- Combined therapy with dapagliflozin and linagliptin demonstrated significant improvements in glycemic parameters (HbA1c, FPG, and PPG) and reduction in body weight among adults with T2DM.
- The combination therapy was well tolerated, with no increase in adverse events, supporting its efficacy and safety as a dual antidiabetic treatment option.

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