International Journal of Current Science Research and Review
ISSN: 2581-8341
Volume 06 Issue 03 March 2023
DOI: 10.47191/ijcsrr/V6-i3-19, Impact Factor: 6.789
IJCSRR @ 2023
www.ijcsrr.org

The Use of Vildagliptin-Dapagliflozin Fixed Dose Combination in Different Patient Profiles in Indian Settings: An Opinion-Based Consensus

Dr. Ritesh Kumar Agrawala[1], Dr. SS Akbar[2], Dr. Kaushik Biswas[3], Dr. Nithin Reddy Modhugu[4], Dr. Umesh Kumar Garg[5], Dr. Sona Warrier[6], Dr. Ashish Prasad[6], Dr. Ashish Birla[6]

[1] Senior Consultant AMRI Hospital, Bhubaneswar
[2] Consultant Physician and Diabetologist, Diabetes Care Clinic, Aligarh
[3] Senior Consultant Endocrinologist, Medica Super specialty Hospital, Kolkata
[4] Consultant Endocrinologist, AIG hospital, Gachibowli, Hyderabad
[5]Consultant Endocrinologist, Pushpanjali Hospital, Delhi Gate, Agra
[6] Scientific Services, USV Private Limited, Mumbai, Maharashtra, India

ABSTRACT

Objective: To evaluate the opinions of Indian clinical experts and aid in clinical choices for the optimal use of vildagliptin-dapagliflozin fixed-dose combination (FDC) for treating type 2 diabetes (T2D) in Indian patients.

Methods: The virtual round table meetings (RTMs) were conducted with healthcare professionals (HCPs) across India. A questionnaire that highlighted the role of vildagliptin-dapagliflozin FDC in treating T2D and determining the correct patient profile was created. The experts held the questionnaire discussion, and their comments were documented. The collected data were evaluated and categorized into four grades: Level A, very strong (≥80% responses); Level B, strong (≥50-79% responses); Level C, moderate (25-49% responses); Level D, neutral/no consensus (<25% responses).

Results: More than 200 HCPs participated in 15 RTMs held between July 15 and October 22, 2022. With a consensus level A (Very strong), HCPs believed that vildagliptin-dapagliflozin FDC is an attractive option and suitable for a wide range of Indian T2D patient profiles, including those with atherosclerotic cardiovascular disease (ASCVD), those with a history of heart failure, older and obese individuals. The experts regarded vildagliptin-dapagliflozin FDC as the first-line treatment for T2D patients who were obese and hypertensive, with a consensus level of C (Moderate). Vildagliptin-dapagliflozin FDC was recommended as second-line treatment for obese and hypertensive T2D patients who are uncontrolled on metformin by experts with consensus level B (Strong). The clinical experts at consensus level B (Strong) agreed that T2D patients taking two oral antidiabetic drugs (OADs) and uncontrolled if HbA1c > 8% might be suitable candidates for initiating vildagliptin-dapagliflozin FDCs.

Conclusion: Based on the present expert opinion-based consensus, most clinical experts believe that vildagliptin - dapagliflozin FDC is an appealing treatment option for a broad range of Indian T2D patients. Nevertheless, more multicentric studies are needed to support these recommendations.

KEYWORDS: Dapagliflozin, FDC, Hypertension Vildagliptin, Obese, T2D

INTRODUCTION

There are 77 million patients with type 2 diabetes (T2D) in India, making it the second-largest diabetes population in the world. The shift in diabetes onset to younger age groups is a particularly concerning trend in India [1]. A series of physiological defects known as "ominous octet" characterize T2D, which includes decreased insulin secretion, reduced insulin sensitivity, increased hepatic glucose synthesis, decreased responses to incretin hormones, increased lipolysis, excess glucagon secretion, increased renal reabsorption of glucose and dysregulation of neurotransmitter. As a result, patients with T2D often require combination therapy since monotherapy cannot address all pathophysiological pathways. Further, it is necessary to ensure that the drug combination targets reversing known pathogenic abnormalities and improves metabolic health rather than simply reducing glycated hemoglobin (HbA1c) levels [2]. In this situation, a rational and synergistic fixed-dose combination (FDC) of antidiabetic medications could be wise to consider. Combination therapy with two drugs may facilitate faster target HbA1c achievement than monotherapy, lessen pill load and boost compliance [1].

International Journal of Current Science Research and Review
ISSN: 2581-8341
Volume 06 Issue 03 March 2023
DOI: 10.47191/ijcsrr/V6-i3-19, Impact Factor: 6.789
IJCSRR @ 2023
www.ijcsrr.org

A combination of sodium-glucose cotransporter type 2 inhibitors (SGT2i) and dipeptidyl peptidase-4 inhibitors (DPP4i) seems promising [3]. SGLT2i reduces hyperglycemia by increasing urine glucose excretion without altering insulin secretion or action. In addition to enhancing glucose homeostasis, DPP4i, which prevents the breakdown of active incretin hormones, increases insulin secretion and lowers glucagon secretion [4]. The combination of a DPP-4i and an SGLT2i is rational not only because they have complementary action but also because they target at least six of the eight components in the "ominous octet" [1]. Additionally, they rarely cause the same adverse effects as other oral hypoglycemic agents, such as weight gain and hypoglycemia [4].

Among the DPP-4i, Vildagliptin has been extensively studied for its clinical utility. Its efficacy profile, low risk of hypoglycemia, lack of weight gain, and absence of an increased risk of cardiovascular (CV) events have made vildagliptin an effective anti-diabetes agent. Across multiple clinical trials, vildagliptin showed a similar safety and tolerability profile to a placebo, and real-life data in patients with T2D supported this [5].

As a highly potent and reversible SGLT2i, dapagliflozin is > 1400 times more selective for SGLT2 than SGLT1, the primary transporter responsible for glucose absorption in the gut. Many patients have shown effective glycemic control and reduced blood pressure and body weight with dapagliflozin when used alone or in combination with other antihyperglycemic agents. Recently, dapagliflozin has become a topic of interest due to its benefits in patients with established atherosclerotic CV disease (ASCVD) or multiple risk factors for CVD outcome trials beyond other antidiabetic drugs. With its antihyperglycemic, cardioprotective, and perhaps renoprotective properties while maintaining a generally favorable tolerability profile, dapagliflozin can treat a wide range of patients, regardless of their CVD history [6].

These advantages have been leveraged by combining vildagliptin and dapagliflozin in a single pill. However, there is a lack of data about its application in Indian patients. Hence, expert discussions were conducted in Indian settings to determine the best use of vildagliptin dapagliflozin FDC considering different T2D patient profiles. A consensus was developed based on this discussion.

METHOD

Healthcare practitioners (HCPs) opinions were recorded based on virtual round table meetings (RTMs) conducted between July 15, 2022, to October 22, 2022. A total of 15 RTMs were conducted, and HCPs from the different geographical regions of PAN India sites participated in these RTMs. A standard questionnaire about vildagliptin-dapagliflozin FDC in T2D management was prepared. The questionnaire included five questions, mainly emphasizing the place of vildagliptin-dapagliflozin FDC in T2D management and identifying a suitable patient profile for this combination (Table 1). All the HCPs were independently requested to vote from the options for each question during the RTMs. The questionnaire was discussed, and thoughts by the experts were recorded for further reference. All the insights were captured, comprehensively reviewed, and discussed to derive the final expert recommendations.

Table 1: Questionnaire for the Consensus

	Question	**Options**
1.	Do you believe that an FDC of vildagliptin-dapagliflozin is an attractive option in today's treatment algorithm of T2D?	A. Yes B. No C. Maybe
2.	In obese people with T2D, the current choice of therapy is SGLT2i; where do you see the place of vildagliptin-dapagliflozin FDC in these patients?	A. As a first-line therapy B. As a second-line therapy – uncontrolled on metformin C. As a third-line therapy – uncontrolled on two OADs
3.	In people with T2D and hypertension, where do you see the place of vildagliptin-Dapagliflozin FDC?	D. As a first-line therapy E. As a second-line therapy – uncontrolled on metformin F. As a third-line therapy – uncontrolled on two OADs

International Journal of Current Science Research and Review
ISSN: 2581-8341
Volume 06 Issue 03 March 2023
DOI: 10.47191/ijcsrr/V6-i3-19, Impact Factor: 6.789
IJCSRR @ 2023
www.ijcsrr.org

4.	Following are a few broad patient profiles; which patients represent the most suitable candidates for vildagliptin-dapagliflozin FDC?	A. T2D patient with ASCVD B. T2D patient with a history of heart failure C. Elderly T2D patient D. Obese T2D patient E. All of the above
5.	In people with T2D who are on two OADs and uncontrolled, at what HbA1c level would you consider initiating a vildagliptin-dapagliflozin FDC?	A. >7% B. >8% C. >8.5% D. >9%
ASCVD: Atherosclerotic cardiovascular disease; FDC: Fixed dose combination; OADs: Oral antidiabetic drugs; T2D: Type 2 diabetes.		

Level of evidence and consensus

Based on the expert's responses, four grades were assigned to the consensus (Table 2). Level A - Very strong (if ≥80% of responses, experts accepted completely); Level B - Strong (If ≥50-79% of responses, experts accepted with minor reservation); Level C - Moderate (If 25-49% of responses, experts accepted with major reservation); Level D - Neutral/ no consensus (If <25% responses, experts rejected the statement).

Table 2: Level of evidence and consensus

Grade	Level of consensus	Voting description	Responses (%)	Description
A	Very strong	Strongly agree + Agree	≥80	Accepted completely
B	Strong	Strongly agree + Agree	≥50-79	Accepted with minor reservation
C	Moderate	Strongly agree + Agree	25-49	Accepted with minor reservation
D	Neutral/ no consensus	Disagree	<25	Rejected

RESULTS

There were more than ~200 HCPs in attendance at the RTMs. The HCP included consulting physicians, diabetologists, endocrinologists, cardiologists, and family physicians. There was strong agreement among the experts that vildagliptin–dapagliflozin FDC is an attractive treatment option in today's treatment algorithm of T2D. Almost 82% (Consensus level A: Very strong) of clinicians regarded vildagliptin–dapagliflozin FDC as an attractive option (Figure 1).

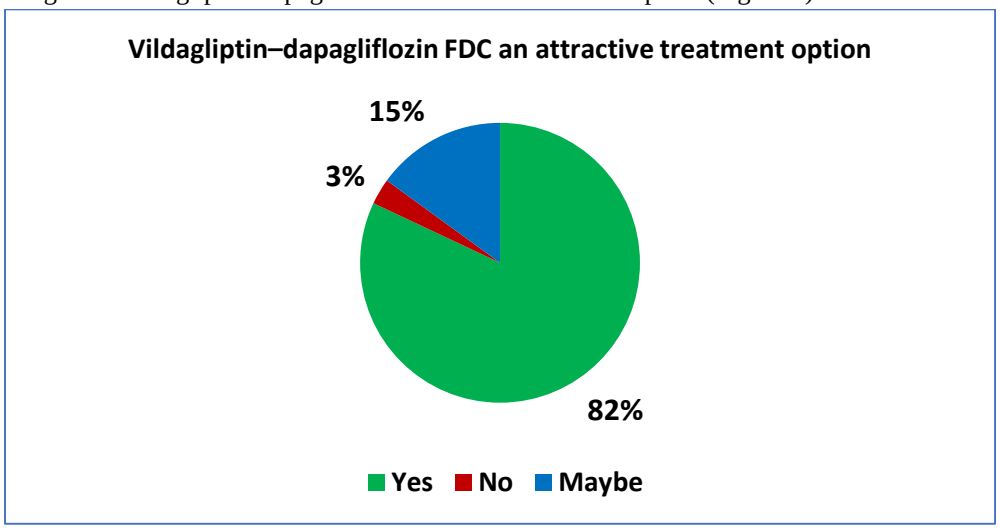

Figure 1: Expert opinions on vildagliptin–dapagliflozin FDC as an attractive treatment.
FDC: Fixed dose combination; T2D: Type 2 diabetes.

International Journal of Current Science Research and Review
ISSN: 2581-8341
Volume 06 Issue 03 March 2023
DOI: 10.47191/ijcsrr/V6-i3-19, Impact Factor: 6.789
IJCSRR @ 2023
www.ijcsrr.org

A modest 48% (Consensus level C: Moderate) of clinicians agreed that vildagliptin-dapagliflozin FDC could be used as a first-line therapy in obese T2D patients where the current choice of treatment is SGLT2i**.** In comparison, 52% (Consensus level B: Strong) considered it second-line therapy in obese T2D patients who are uncontrolled on metformin (Figure 2).

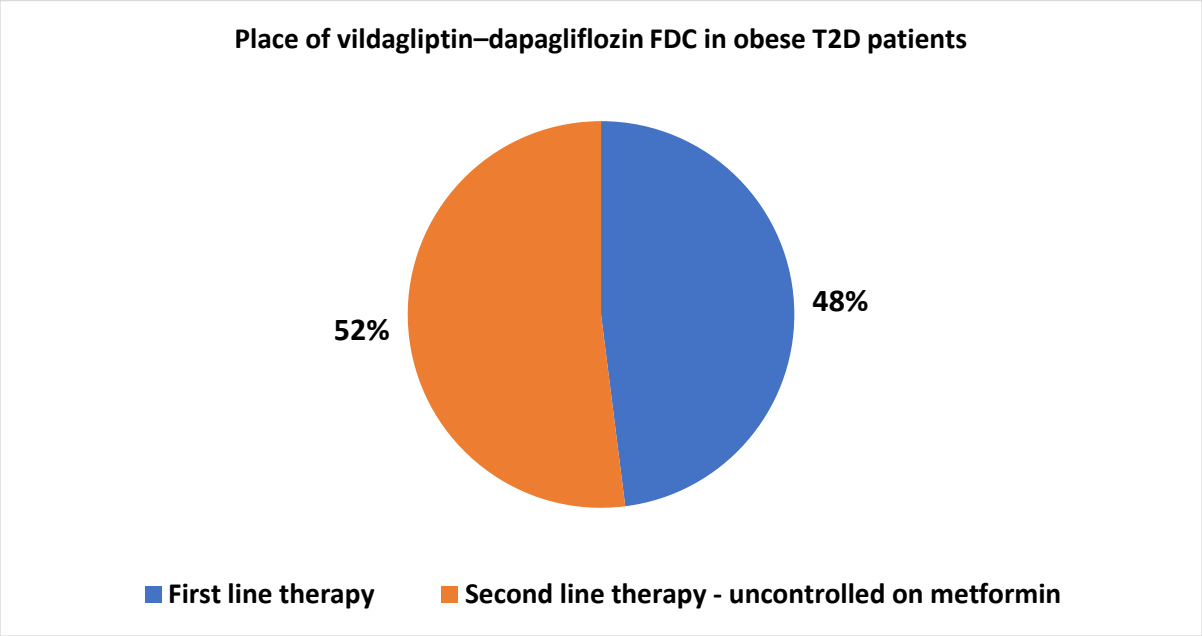

Figure 2: Expert opinion on the place of vildagliptin-dapagliflozin FDC in obese patients with T2D.
FDC: Fixed dose combination; T2D: Type 2 diabetes.

According to 43% of experts (Consensus level C: Moderate), vildagliptin-dapagliflozin FDC can be used as a first-line therapy in T2D patients with hypertension. At the same time, 53% (Consensus level B: Strong) considered it second-line treatment in T2D patients with hypertension who are uncontrolled on metformin (Figure 3).

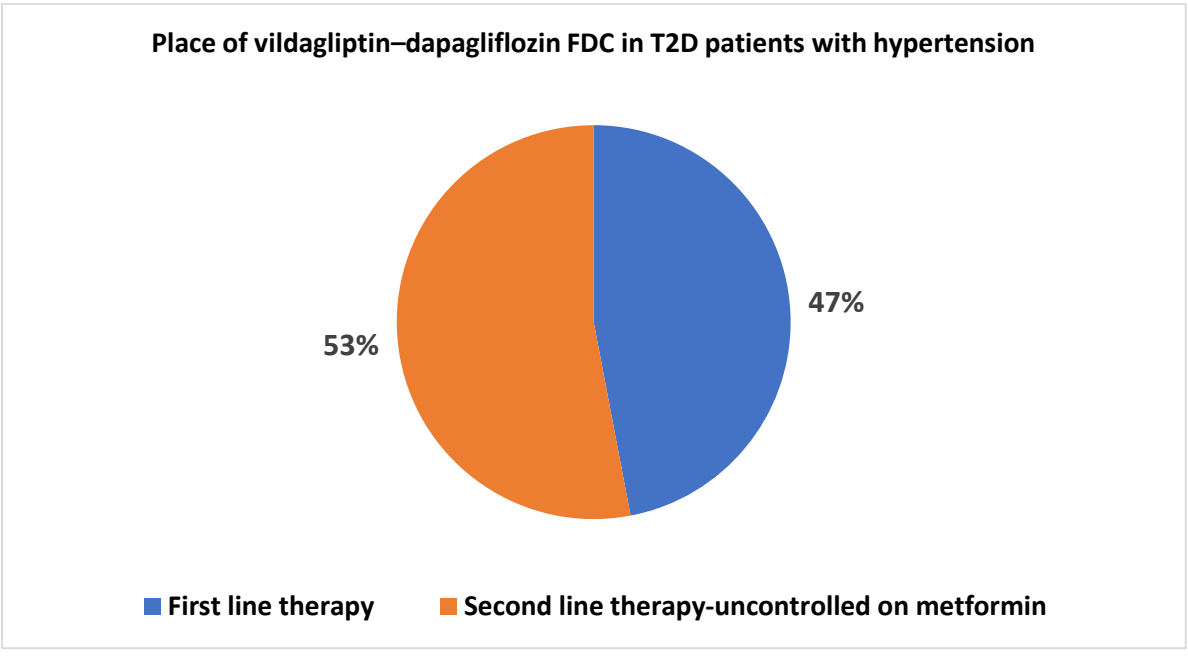

Figure 3: Expert opinions on vildagliptin-dapagliflozin FDC in T2D patients with hypertension.
FDC: Fixed dose combination; T2D: Type 2 diabetes.

International Journal of Current Science Research and Review
ISSN: 2581-8341
Volume 06 Issue 03 March 2023
DOI: 10.47191/ijcsrr/V6-i3-19, Impact Factor: 6.789
IJCSRR @ 2023
www.ijcsrr.org

The experts strongly believed that vildagliptin-dapagliflozin FDC is appropriate for a wide range of T2D patient profiles. Nearly 89% (Consensus level A: very strong) clinicians agreed that T2D patients with ASCVD, T2D patients with a history of heart failure, and elderly and obese T2D patients all are suitable candidates for vildagliptin-dapagliflozin FDC (Figure 4).

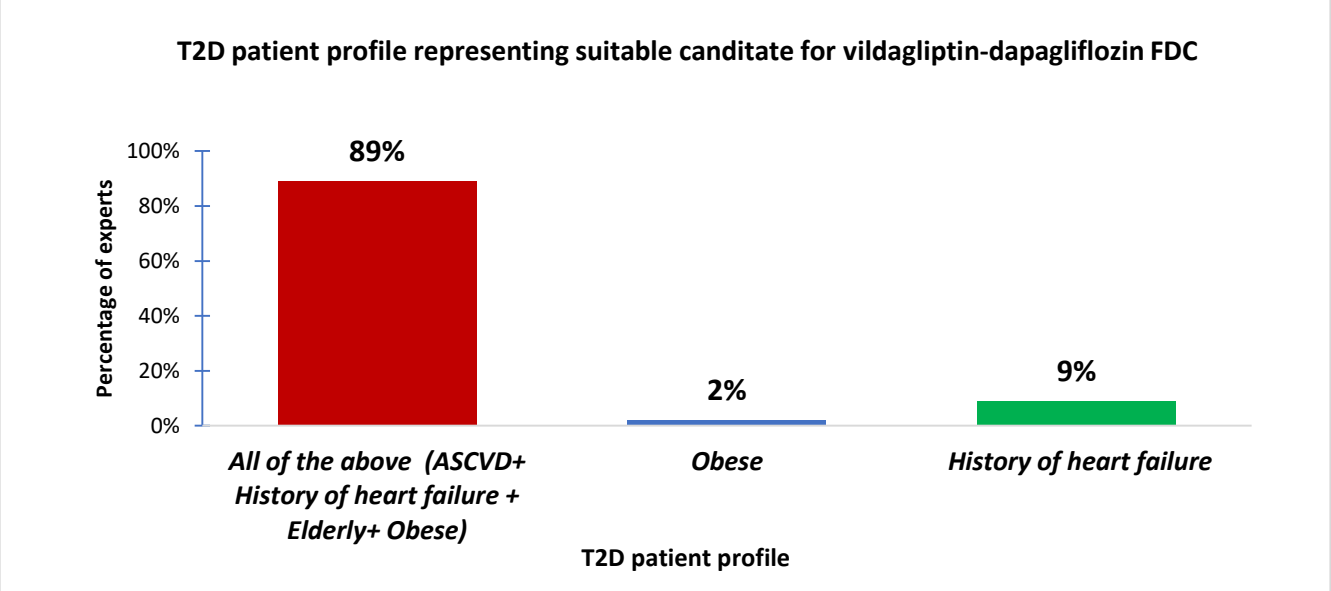

Figure 4: Expert opinions on which profile of T2D patients is most suitable for vildagliptin-dapagliflozin FDC**.**
ASCVD: Atherosclerotic cardiovascular disease; FDC: Fixed dose combination; T2D: Type 2 diabetes.

Approximately 53% (Consensus level B: Strong) of clinicians held the opinion that T2D patients taking two oral antidiabetic drugs (OADs) and uncontrolled if the HbA1c levels are > 8% then they are suitable candidates for starting vildagliptin-dapagliflozin FDCs. As per 27% (Consensus level C: Moderate) of the respondents, the use of vildagliptin-dapagliflozin FDCs can be considered in these patients if their HbA1c levels are > 7% (Figure 5).

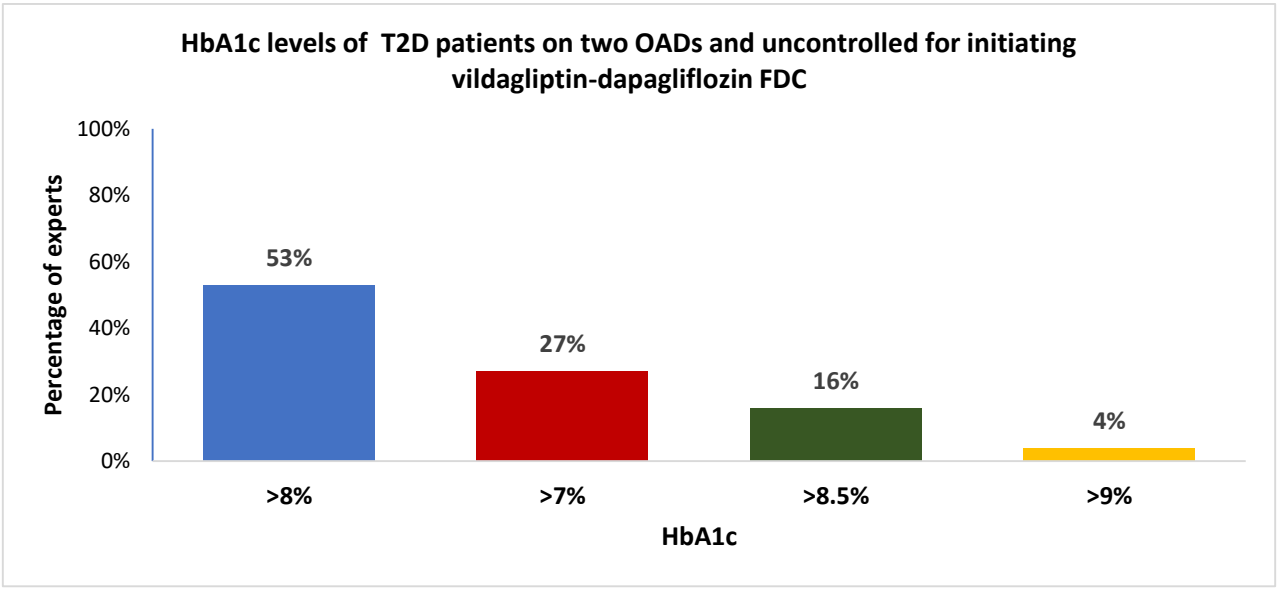

Figure 5: Expert opinions on HbA1c levels of T2D patients on two OADs and uncontrolled for initiating vildagliptin-dapagliflozin FDC.
FDC: Fixed dose combination; OADs: Oral antidiabetic drugs; T2D: Type 2 diabetes.

International Journal of Current Science Research and Review
ISSN: 2581-8341
Volume 06 Issue 03 March 2023
DOI: 10.47191/ijcsrr/V6-i3-19, Impact Factor: 6.789
IJCSRR @ 2023
www.ijcsrr.org

DISCUSSION

The purpose of this expert opinion was to assist clinicians in making clinical decisions regarding the appropriate use of vildagliptin-dapagliflozin FDC for the treatment of T2D. SGLT2i + DPP4i FDCs have been available in India since 2018, but unlike metformin-based FDCs, these do not have a clear position in T2D management [1]. Thus, an expert discussion was conducted to address the existing gaps, and a consensus was developed.

Most experts (82%) agreed that vildagliptin–dapagliflozin FDC is an attractive treatment option for T2D today. DPP-4i and SGLT2i are attractive in combination because they have complementary modes of action that contribute to better blood glucose control in patients with T2D without compromising their safety/tolerance profiles; in contrast, some adverse events are expected to be reduced [3].In light of findings that SGLT2i, like dapagliflozin, produces glucosuria, which is associated with an increase in endogenous glucose production that offsets the glucose-lowering effect by approximately 50%, this combination is particularly appealing. As DPP-4i, like vildagliptin, inhibit glucagon secretion and reduces endogenous glucose production, According to these findings, the combination of an SGLT2i with a DPP-4i may improve the ability of individuals with T2D to achieve their glycemic goal and synergistically reduce HbA1c [7,8].

The benefits of vildagliptin – dapagliflozin FDC extend far beyond glycemic control. The present survey revealed that many HCPs considered vildagliptin-dapagliflozin FDC as the initial therapy for obese T2D patients. For the treatment of T2D, currently available FDCs comprise metformin with another drug which may cause adverse effects such as gastrointestinal, weight gain, hypoglycemia, increased fluid retention, and other adverse effects. DPP-4i and SGLT2i are inherently resistant to these side effects. Further, clinically meaningful weight reductions have been observed with SGLT2i alone and in combination with DPP-4i. An FDC containing a DPP-4i - SGLT2i might be a desirable treatment for people who are overweight or obese [9]. Numerous monotherapy and combination trials have proven that vildagliptin is weight neutral for T2D patients. Vildagliptin's glucose-dependent mechanism of action leads to a low risk of hypoglycemia, which may contribute to its weight neutrality by preventing "defensive eating"[10]. With dapagliflozin, weight loss may be caused by lower body fat due to caloric restriction, fluid loss due to osmotic diuresis, or a combination of the two [11]. Dapagliflozin has reportedly been linked to a 2.7–3.2 kg weight loss in T2D patients [12].

The use of vildagliptin-dapagliflozin FDC as first-line therapy in T2D patients with hypertension was generally agreed upon by Indian clinicians in the survey with a moderate consensus level. There is evidence that vildagliptin reduces vascular stiffness via the elevation of nitric oxide synthesis, improves vascular relaxation, and reduces systolic blood pressure. (SBP) and diastolic blood pressure (DBP) [13]. A large pooled analysis showed that vildagliptin treatment for 24 weeks significantly reduced SBP by - 2.70 mmHg and DBP by - 1.64 mmHg [14]. Dapagliflozin also lowers blood pressure (BP) in patients with T2D [15]. Dapagliflozin-induced plasma volume contraction contributes to the initial reduction in systolic blood pressure (SBP). Conversely, a reduction in sympathetic nervous system activity may contribute to persistently lower SBP. Ten days of dapagliflozin treatment has been shown to reduce SBP by − 4.7 mmHg and by − 4.4 mmHg after 16 weeks [16].

Most clinicians strongly endorsed vildagliptin-dapagliflozin FDC in a wide range of patients with T2D. Patients with ASCVD, a history of heart failure, and the elderly and obese all were considered for this combination.

Studies have highlighted the cardioprotective effect of SGLT-2i, like dapagliflozin, in diabetics and non-diabetics patients with established CVD [17]. DECLARE–TIMI 58, a large trial that assessed CV outcomes with dapagliflozin, showed that in patients with T2D who had or were at risk for ASCVD, treatment with dapagliflozin did result in a lower rate of CV death or hospitalization for heart failure [18]. In the DAPA-HF trial among patients with heart failure and a reduced ejection fraction, the risk of worsening heart failure or death from CV causes was lower among those who received dapagliflozin than among those who received a placebo, regardless of the presence or absence of diabetes [19]. Vildagliptin's CV safety has been demonstrated by a large meta-analysis of 17000 patients where it was not associated with an increased risk of adjudicated major CV events relative to comparators. Moreover, this analysis did not find a significantly increased risk of heart failure in vildagliptin-treated patients [20]. A real-world study comparing vildagliptin to other OADs found no evidence of a higher overall CVD risk or a risk of myocardial infarction, acute coronary syndrome, stroke, or congestive heart failure [21].

Experts widely agreed that patients with HbA1c >8% uncontrolled on two OADs should initiate vildagliptin-dapagliflozin FDC. The inclusion criteria of the SGLT2i + DPP4i FDC randomized control trial suggest that in treatment-naïve T2D patients for whom metformin is contraindicated or who are metformin intolerant with HbA1c > 8 % and in patients uncontrolled on metformin with HbA1c of > 8.5% this FDC can be initiated along with lifestyle modification [1].

International Journal of Current Science Research and Review
ISSN: 2581-8341
Volume 06 Issue 03 March 2023
DOI: 10.47191/ijcsrr/V6-i3-19, Impact Factor: 6.789
IJCSRR @ 2023
www.ijcsrr.org

CONCLUSION

According to the current consensus of expert opinion, most clinical experts think that vildagliptin-dapagliflozin FDC is a promising therapeutic option for a broad range of T2D Indian patients. It is a suitable option for Indian T2D patients as it synergistically improves individuals' ability to achieve their glycemic targets, offers multiple extra glycemic advantages, including body weight reduction, BP lowering, and cardioprotective effects. However, multicentric studies are necessary to confirm the advantages and disadvantages of the vildagliptin-dapagliflozin FDC.

Key Recommendations

Vildagliptin–Dapagliflozin FDC - Statement	Level of Consensus
An attractive treatment option in today's treatment algorithm of T2D.	Very strong (Level A)
First-line therapy in obese T2D patients	Moderate (Level C)
Second-line therapy in obese T2D patients who are uncontrolled on metformin	Strong (Level B)
First-line therapy in T2D patients with hypertension	Moderate (Level C)
Second-line therapy in T2D patients with hypertension who are uncontrolled on metformin	Strong (Level B)
Suitable for a broad range of T2D patients (ASCVD, heart failure, obese, elderly)	Very strong (Level A)
T2D patients taking two OADs and uncontrolled with HbA1c levels > 8% are suitable candidates	Strong (Level B)

REFERENCES

1. Chadha M, Das AK, Deb P, Gangopadhyay KK, Joshi S, Kesavadev J, Kovil R, Kumar S, Misra A, Mohan V. Expert Opinion: Optimum Clinical Approach to Combination-Use of SGLT2i + DPP4i in the Indian Diabetes Setting. Diabetes Ther. 2022 May;13(5):1097-1114.
2. Kalra S, Kesavadev J, Chadha M, Kumar GV. Sodium-glucose Cotransporter-2 Inhibitors in Combination with Other Glucose-lowering Agents for the Treatment of Type 2 Diabetes Mellitus. Indian J Endocrinol Metab. 2018 Nov-Dec;22(6):827-836.
3. Scheen AJ. DPP-4 inhibitor plus SGLT-2 inhibitor as combination therapy for type 2 diabetes: from rationale to clinical aspects. Expert Opin Drug Metab Toxicol. 2016 Dec;12(12):1407-1417.
4. Min SH, Yoon JH, Moon SJ, Hahn S, Cho YM. Combination of sodium-glucose cotransporter 2 inhibitor and dipeptidyl peptidase-4 inhibitor in type 2 diabetes: a systematic review with meta-analysis. Sci Rep. 2018 13th March;8(1):4466.
5. Mathieu C, Kozlovski P, Paldánius PM, Foley JE, Modgill V, Evans M, Serban C. Clinical Safety and Tolerability of Vildagliptin - Insights from Randomised Trials, Observational Studies and Post-marketing Surveillance. Eur Endocrinol. 2017 Aug;13(2):68-72.
6. Dhillon S. Dapagliflozin: A Review in Type 2 Diabetes. Drugs. 2019 Jul;79(10):1135-1146.
7. Abdul-Ghani M. Where does combination therapy with an SGLT2 inhibitor plus a DPP-4 inhibitor fit in the management of type 2 diabetes? Diabetes Care. 2015 Mar;38(3):373-5.
8. Sharma MD. Potential for combination of dipeptidyl peptidase-4 inhibitors and sodium-glucose co-transporter-2 inhibitors for the treatment of type 2 diabetes. Diabetes Obes Metab. 2015 Jul;17(7):616-21.
9. Singh-Franco D. Potential for dipeptidyl peptidase-4 inhibitor and sodium glucose cotransporter 2 inhibitor single-pill combinations. Expert Rev Endocrinol Metab. 2015 May;10(3):305-317.
10. Foley JE, Jordan J. Weight neutrality with the DPP-4 inhibitor, vildagliptin: mechanistic basis and clinical experience. Vasc Health Risk Manag. 2010 9th August;6:541-8.
11. Bolinder J, Ljunggren Ö, Kullberg J, Johansson L, Wilding J, Langkilde AM, Sugg J, Parikh S. Effects of dapagliflozin on body weight, total fat mass, and regional adipose tissue distribution in patients with type 2 diabetes mellitus with inadequate glycemic control on metformin. J Clin Endocrinol Metab. 2012 Mar;97(3):1020-31.
12. Williams DM, Nawaz A, Evans M. Drug Therapy in Obesity: A Review of Current and Emerging Treatments. Diabetes Ther. 2020 Jun;11(6):1199-1216.

International Journal of Current Science Research and Review
ISSN: 2581-8341
Volume 06 Issue 03 March 2023
DOI: 10.47191/ijcsrr/V6-i3-19, Impact Factor: 6.789
IJCSRR @ 2023
www.ijcsrr.org

13. Wiciński M, Górski K, Wódkiewicz E, Walczak M, Nowaczewska M, Malinowski B. Vasculoprotective Effects of Vildagliptin. Focus on Atherogenesis. Int J Mol Sci. 2020 Mar 25;21(7):2275.
14. Evans M, Schweizer A, Foley JE. Blood pressure and fasting lipid changes after 24 weeks treatment with vildagliptin: a pooled analysis in >2,000 previously drug-naïve patients with type 2 diabetes mellitus. Vasc Health Risk Manag. 2016 18th August;12:337-40.
15. Sjöström CD, Johansson P, Ptaszynska A, List J, Johnsson E. Dapagliflozin lowers blood pressure in hypertensive and non-hypertensive patients with type 2 diabetes. Diab Vasc Dis Res. 2015 Sep;12(5):352-8.
16. van Ruiten CC, Smits MM, Kok MD, Serné EH, van Raalte DH, Kramer MHH, Nieuwdorp M, IJzerman RG. Mechanisms underlying the blood pressure lowering effects of dapagliflozin, exenatide, and their combination in people with type 2 diabetes: a secondary analysis of a randomized trial. Cardiovasc Diabetol. 2022 Apr 28;21(1):63.
17. Rehman SU, Rahman F. Evidence-Based Clinical Review on Cardiovascular Benefits of SGLT2 (Sodium-Glucose Co-Transporter Type 2) Inhibitors in Type 2 Diabetes Mellitus. Cureus. 2020 Aug 11;12(8):e9655.
18. Wiviott SD, Raz I, Bonaca MP, Mosenzon O, Kato ET, Cahn A, Silverman MG, Zelniker TA, Kuder JF, Murphy SA, Bhatt DL, Leiter LA, McGuire DK, Wilding JPH, Ruff CT, Gause-Nilsson IAM, Fredriksson M, Johansson PA, Langkilde AM, Sabatine MS; DECLARE–TIMI 58 Investigators. Dapagliflozin and Cardiovascular Outcomes in Type 2 Diabetes. N Engl J Med. 2019 Jan 24;380(4):347-357.
19. McMurray JJV, Solomon SD, Inzucchi SE, Køber L, Kosiborod MN, Martinez FA, Ponikowski P, Sabatine MS, Anand IS, Bělohlávek J, Böhm M, Chiang CE, Chopra VK, de Boer RA, Desai AS, Diez M, Drozdz J, Dukát A, Ge J, Howlett JG, Katova T, Kitakaze M, Ljungman CEA, Merkely B, Nicolau JC, O'Meara E, Petrie MC, Vinh PN, Schou M, Tereshchenko S, Verma S, Held C, DeMets DL, Docherty KF, Jhund PS, Bengtsson O, Sjöstrand M, Langkilde AM; DAPA-HF Trial Committees and Investigators. Dapagliflozin in Patients with Heart Failure and Reduced Ejection Fraction. N Engl J Med. 2019 Nov.
20. McInnes G, Evans M, Del Prato S, Stumvoll M, Schweizer A, Lukashevich V, Shao Q, Kothny W. Cardiovascular and heart failure safety profile of vildagliptin: a meta-analysis of 17 000 patients. Diabetes Obes Metab. 2015 Nov;17(11):1085-92.
21. Williams R, de Vries F, Kothny W, Serban C, Lopez-Leon S, Chu C, Schlienger R. Cardiovascular safety of vildagliptin in patients with type 2 diabetes: A European multi-database, non-interventional post-authorization safety study. Diabetes Obes Metab. 2017 Oct;19(10):1473-1478.

Cite this Article: Dr. Ritesh Kumar Agrawala, Dr. SS Akbar, Dr. Kaushik Biswas, Dr. Nithin Reddy Modhugu, Dr. Umesh Kumar Garg, Dr. Sona Warrier, Dr. Ashish Prasad, Dr. Ashish Birla (2023). The Use of Vildagliptin-Dapagliflozin Fixed Dose Combination in Different Patient Profiles in Indian Settings: An Opinion-Based Consensus. International Journal of Current Science Research and Review, 6(3), 2010-2017