Teneligliptin Real-World Effectiveness Assessment in Patients with Type 2 Diabetes Mellitus in India: A Retrospective Analysis (TREAT-INDIA 2)

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ABSTRACT

Introduction: Teneligliptin is an antidiabetic medication that has been approved for the management of type 2 diabetes mellitus (T2DM) in Japan, South Korea and India. It is one of the most commonly prescribed antihyperglycaemic agents. The aim of this study was to assess the effectiveness of teneligliptin in improving glycemic control amongst Indian patients with T2DM in a real-world setting.

Methods: This was a retrospective observational study in which a predesigned structured proforma was used to collect information from hospital records of 18 medical centres across India. All participating centres were established primary care hospitals with adequate record keeping, a pre-determined condition in the study design. Data were collected during the period of January 2019 to June 2019. Data extracted from patient records, including glycaemic parameters, concomitant drugs, drug dosage and duration, were collated. The effectiveness of teneligliptin was assessed by analyzing the mean change in glycosylated haemoglobin (HbA1c), fasting plasma glucose (FPG) and post-prandial plasma glucose (PPG) at 12 weeks after initiation of teneligliptin.

Results: Data from 10,623 patients were available for analysis. The mean age of the enrolled patients was 51.86 ± 11.76 years. At 12 weeks after initiation of teneligliptin as monotherapy or add-on to other medications (combination therapy), the patients showed a significant decrease from baseline in mean HbA1c, FPG and PPG. Mean HbA1c dropped from 8.66 ± 1.15% at baseline to 7.67 ± 1.28% at 12 weeks (71 ± 12.6 to 60 ± 14 mmol/mol), with a difference of −0.99% (95% confidence interval [CI] 0.96–1.02) or −10.8 (95% CI 10.5–11.1) mmol/mol (p < 0.0001). The mean reductions in FPG and PPG were 43.12 mg/dL (2.39 mmol/L) and 87.73 mg/dL (4.87 mmol/L) (both p < 0.0001) respectively. HbA1c (%) reductions
with teneligliptin when used as add-on to metformin, add-on to metformin + sulfonylurea combination and add-on to metformin + sulfonylurea + alpha glucosidase inhibitor combination were 0.76% (8.3 mmol/mol), 1.24% (13.6 mmol/mol) and 1.04% (11.4 mmol/mol), respectively. Teneligliptin also significantly reduced HbA1c (1.13% or 12.4 mmol/mol, \( p < 0.0001 \)) in patients with impaired renal function, without worsening the estimated glomerular filtration rate. Teneligliptin consistently reduced HbA1c across all three age categories tested—by 1% (10.9 mmol/mol) in patients aged < 60 years, by 1.15% (12.6 mmol/mol) in patients aged 60–75 years and by 0.88% (9.6 mmol/mol) in patients aged > 75 years.

**Conclusion:** Teneligliptin significantly improved glycaemic parameters in Indian patients with T2DM when prescribed either as monotherapy or as an add-on to one or more other commonly prescribed antihyperglycaemic agents.

**Keywords:** Diabetes mellitus; DPP4I; HbA1c; Teneligliptin

**Key Summary Points**

There are a limited number of drug utilization studies of teneligliptin in real-world settings despite this medication being a commonly prescribed gliptin in India for the management of type 2 diabetes mellitus (T2DM).

We collected and analysed the data of > 10,000 patients for changes in the glycemic parameters following treatment with teneligliptin as monotherapy and as add-on with other oral antihyperglycaemic agents (combination therapy).

The effectiveness of teneligliptin was evaluated as monotherapy and in combination therapy in the whole patient population, as well as in sub-analyses according to age, renal impairment and insulin therapy.

Teneligliptin, either as monotherapy or as an add-on therapy, significantly improved glycaemic parameters, leading to the conclusion that it can be considered as an effective add-on antidiabetic agent in the management of Indian patients with T2DM.

Although a cause-and-effect relationship cannot be determined using data from retrospective studies due to limited access, our results are useful by providing preliminary data and guiding the development of future prospective long-term studies.

**INTRODUCTION**

Type 2 diabetes mellitus (T2DM) is a global pandemic, and India is steadily emerging as the diabetes capital of world [1]. The number of patients with diabetes in India is likely to reach 134.2 million by 2045 [2]. This relatively recent increase in prevalence of T2DM can be attributed to multiple factors [3].

Management of T2DM entails lifestyle changes and pharmacological therapy, with the latter ideally meeting the criteria of being efficacious, durable, safe and cost effective. Dipeptidyl peptidase-4 inhibitors (DPP-4Is; also known as “gliptins”) are a relatively novel class of antihyperglycaemic agents widely used in the management of T2DM [4]. Although the mechanism of action of all DPP-4Is is same, individual gliptins may differ from each other in terms of their pharmacokinetics, pharmacodynamics and potency [5].

Teneligliptin is a class 3 DPP4I with a unique structure [6] that enhances its potency and selectivity, such that it has a fivefold higher activity than other gliptins and produces more extensive inhibition of DPP-4 [7]. It has been available in India since 2015 and is widely used both as monotherapy and in combination with other medications. In addition to its high potency and selectivity, teneligliptin is available at an affordable cost and, consequently, it is very commonly prescribed in India. At the time
of initiating the study reported here, teneligliptin was the cheapest gliptin available in India.

Drug utilization studies of teneligliptin in real-world settings are limited despite it being a commonly prescribed gliptin in India. While studies in India have reported real-world evidence (RWE) of teneligliptin, they are not as extensive as the analysis of data from the case report forms (CRFs) of the post-marketing surveillance (RUBY surveillance) conducted by Kadowaki et al. in patients with T2DM in a large Japanese population [8]. Such large-scale studies are needed to understand the factors influencing the management of diabetes in the real-world setting.

The study reported here was therefore designed to evaluate the effectiveness of teneligliptin in the Indian population in the real-world setting.

METHODS

This was a retrospective audit/analysis in which a predesigned CRF was used to collate patient information from hospital/clinic records of 18 centres across India. All participating centres were established primary care hospitals which maintained an adequate level of record keeping as assessed by pre-determined criteria in the study design. Data were collected from January 2019 to June 2019. Patients with T2DM who were aged ≥18 years and had been treated with teneligliptin for a minimum of 12 weeks (either as monotherapy or in combination with other antidiabetic drugs) were eligible to participate in the study. Patients were excluded if there was any modification in the treatment regimen of other antidiabetic drugs during the 12-week period. Patient details extracted from the medical records included age, gender, concomitant drug or medical history, glycaemic parameters, drug dosage and duration of diabetes. Information was collected either from a hard copy or soft copy of the medical record, and data were collated on CRFs for this study (denoted the TREAT-INDIA 2 study) and analysed further. The effectiveness of teneligliptin was analysed on the basis of mean change in glycaemic parameters, including glycosylated haemoglobin (HbA1c), fasting plasma glucose (FPG) and postprandial plasma glucose (PPG) in the 3-month treatment period. Data were compiled on Microsoft Excel (Microsoft Corp., Redmond, WA, USA) and analysed using SPSS software version 15 (IBM Corp., Armonk, NY, USA). Categorical data were represented in simple percentage and mean ± standard deviation. The paired t test was used to compare change in the glycemic parameters. A p value < 0.05 was considered to be significant.

Prior to collecting patient information approval was obtained from the Institutional Ethics Committee (Suraksha Ethics committee. Reg No: ECR/644/Inst/MH/2014/RR-17). The study was performed in accordance with the Helsinki Declaration of 1964, and its later amendments.

RESULTS

Data from a total of 10,623 patients from 18 hospitals/clinics were analysed; of these 18 participating centres, seven were located in southern India, three were located in eastern India and four each were located in northern and western India. Table 1 shows the baseline demographic and clinical characteristics of the patients. The average age of patients was 51.86 ± 11.76 years, and the male to female ratio was 1.1:1. The duration of T2DM (four categories of duration) and percentage of patients in each duration category were: < 5 years (53% of patients); 5–10 years (33%); 11–15 years (11%); > 15 years (3%). Hypertension (56% of patients) was the most common comorbidity, followed by dyslipidemia (25%), chronic kidney disease (8%), coronary artery disease (6%), chronic liver disease (4%) and stroke (1%).

There was a statistically significant (all p < 0.0001) improvement from baseline in mean HbA1c (−0.99%, 95% confidence interval [CI] 0.96–1.02 or −10.8, [95% CI 10.5–11.1] mmol/mol), FPG (−43.12 mg/dL, 95% CI 42.5–43.7 or −2.39 [95% CI 2.36–2.43] mmol/L) and PPG (−87.73 mg/dL, 95% CI 86.5—88.9 or −4.87 [95% CI 4.8–4.93] mmol/L) at the end of
12 weeks of teneligliptin therapy in the total patient population (Table 2). The glycaemic target of HbA1c ≤ 7%, FPG ≤ 130 mg/dL and PPG ≤ 180 mg/dL was achieved by 35, 81 and 71% of patients, respectively, after 12 weeks of teneligliptin treatment (Table 3). Teneligliptin was prescribed as a monotherapy in 4% of patients and as a part of add-on therapy in 96% patients (Table 1). Of the combination therapies, teneligliptin with metformin was the most common combination prescribed (40%), followed by teneligliptin with metformin and sulfonylureas (SUs), prescribed in 34% patients (Table 1).

Table 4 depicts the change in HbA1c in patients on the different treatment regimens based on baseline HbA1c; it was observed that reductions in HbA1c were greater in patients having higher baseline HbA1c levels. HbA1c (%)

- Teneligliptin Monotherapy, n (%) 390 (4%)
- Teneligliptin + Metformin, n (%) 4299 (40%)
- Teneligliptin + Metformin + sulfonylureas, n (%) 3608 (34%)
- Teneligliptin + Metformin + sulfonylureas + α-glucosidase inhibitors, n (%) 953 (9%)
- Teneligliptin + Insulin + Other oral antidiabetic drugs (OADs)*, n (%) 150 (1%)
- Teneligliptin + Other OADs*, n (%) 1223 (12%)

* Other OADs include Metformin; Sodium glucose co-transporter 2 inhibitors (SGLT2i) = Empagliflozin, Canagliflozin, Dapagliflozin; Sulfonylureas = Gliclazide, Glimepiride, Glipizide; Alpha glucosidase inhibitor (AGIs) = Acarbose; Pioglitazone

T2DM Type 2 Diabetes Mellitus, HbA1c hemoglobin A1c, FPG fasting plasma glucose, PPG postprandial plasma glucose, OADs oral antidiabetic drugs
and 1.04% (11.4 mmol/mol), respectively. Teneligliptin used in conjunction with insulin, with or without other oral antidiabetic drugs (OADs), reduced HbA1c by 1.48% (95% CI 1.21–1.74) or by 16.2 mmol/mol (95% CI 13.2–19.0) \( p < 0.0001 \). There was a statistically significant reduction in all the glycemic parameters with teneligliptin monotherapy and in all combinations of teneligliptin and antidiabetic drugs (Table 5).

The data were subjected to sub-analysis to assess the effectiveness of teneligliptin in specific patient populations, such as patients with impaired renal function (defined as estimated glomerular filtration rate [eGFR] < 60 mL/min/1.73m\(^2\); \( n = 549 \)). In these patients with impaired renal function who were
prescribed teneligliptin, mean changes in HbA1c, FPG, and PPG were $-1.13\%$ (95% CI 1.03–1.22) or $-12.4$ (95% CI 11.3–13.3) mmol/mol ($p < 0.0001$), $-58.71$ mg/dL (95% CI 57.2–60.18) or $-3.26$ (95% CI 3.17–3.34) mmol/L ($p < 0.0001$) and $-92.74$ mg/dL (95% CI 88.85–96.6) or $-5.15$ (CI 4.93–5.36) mmol/L ($p < 0.0001$), respectively (Table 6). No significant changes from baseline in eGFR were observed at 12 weeks after initiating teneligliptin therapy.

Data were also analysed to assess the effectiveness of teneligliptin in various age group categories (< 60 years [n = 7593], 60–75 years [n = 2872], > 75 years [n = 158]). It was observed that after initiation of teneligliptin, there was a significant reduction in all the glycaemic parameters and that this reduction was

### Table 5
Change in the glycaemic parameters from baseline to end of 12-week treatment period with teneligliptin in the study population according to type of therapy (monotherapy or combination therapy)

| Teneligliptin therapy (monotherapy and in combination) | Glycaemic parameters |
|-------------------------------------------------------|----------------------|
|                                                       | FPG (mg/dL) | PPG (mg/dL) | HbA1c (%) |
| Teneligliptin monotherapy (n = 390)                    |             |             |           |
| Baseline                                             | 169.23 ± 23.06 | 246.54 ± 48.65 | 8.38 ± 1.17 |
| 12 Weeks                                             | 129.36 ± 22.61 | 198.24 ± 44.73 | 7.68 ± 1.29 |
| Difference                                           | $-39.87^*$   | $-48.3^*$   | $-0.7^*$ |
| Teneligliptin + metformin (n = 4299)                  |             |             |           |
| Baseline                                             | 160.71 ± 23.06 | 266.31 ± 47.40 | 8.56 ± 1.15 |
| 12 Weeks                                             | 119.21 ± 22.02 | 178.92 ± 43.57 | 7.8 ± 1.28 |
| Difference                                           | $-41.5^*$    | $-87.39^*$  | $-0.76^*$ |
| Teneligliptin + metformin + SUs (n = 3608)            |             |             |           |
| Baseline                                             | 159.96 ± 23.05 | 247.61 ± 47.39 | 8.77 ± 1.15 |
| 12 Weeks                                             | 115.35 ± 22.01 | 154.69 ± 43.57 | 7.53 ± 1.28 |
| Difference                                           | $-44.61^*$   | $-92.92^*$  | $-1.24^*$ |
| Teneligliptin + metformin + SU + AGI (n = 953)        |             |             |           |
| Baseline                                             | 170.68 ± 18.56 | 271.5 ± 46.22 | 8.7 ± 1.09 |
| 12 Weeks                                             | 119.33 ± 19.24 | 178.12 ± 43.19 | 7.66 ± 1.24 |
| Difference                                           | $-51.35^*$   | $-93.38^*$  | $-1.04^*$ |
| Teneligliptin + insulin with or without other OADsa (n = 150) |             |             |           |
| Baseline                                             | 174.53 ± 18.8 | 280.99 ± 46.32 | 8.25 ± 1.09 |
| 12 Weeks                                             | 101.83 ± 19.48 | 178.3 ± 43.32 | 6.77 ± 1.24 |
| Difference                                           | $-72.7^*$    | $-102.69^*$ | $-1.48^*$ |

Values in table are presented as the mean ± SD (where appropriate)

*SU sulfonylureas, AGI alpha glucosidase inhibitor, OADs oral antidiabetic drugs

*Difference is significant at $p < 0.0001$, paired t test

a Other OADs include Metformin; Sodium glucose co-transporter 2 inhibitors (SGLT2i) = Empagliflozin, Canagliflozin, Dapagliflozin; Sulfonylureas = Gliclazide, Glimepiride, Glipizide; Alpha glucosidase inhibitor (AGIs) = Acarbose; Pioglitazone
consistent in all age groups. The reductions in HbA1c in patients aged < 60, 60–75, and > 75 years were 1% (95% CI 0.96–1.03) or 10.9 mmol/mol (95% CI 10.5–11.3) \((p \leq 0.0001)\), 1.15% (95% CI 0.88–1.01) or 12.6 (95% CI 9.6–11.0) mmol/mol \((p \leq 0.0001)\) and 0.88% (95% CI 0.58–1.17) or 9.6 (CI 6.3–12.8) mmol/mol \((p \leq 0.0001)\), respectively (Table 7).

**DISCUSSION**

Real-world data regarding the efficacy of teneligliptin in Indian patients with T2DM are limited. To the best of our knowledge, our study is the largest analysis of real-world data on the use of teneligliptin not just in India, but worldwide, with data of 10,623 patients used to analyse the effectiveness of teneligliptin on various blood glucose parameters. The only other large-scale study conducted to date was a Japanese study involving 10,532 patients [8]. Our data demonstrate the effectiveness of teneligliptin to improve glycaemic control in Indian patients with T2DM. Statistically significant \((p \leq 0.0001)\) improvements in glycemic parameters were observed not only in the overall patient population but also in patients with renal impairment as well as in those in different age groups (i.e. aged < 60 years, 60–75 years and > 75 years).

DPP-4Is, also known as gliptins, are a relatively new class of antidiabetic agents that have revolutionized the management of T2DM [4]. DPP-4Is are usually prescribed in patients who

### Table 6 Change in glycaemic parameters from baseline to end of 12-week treatment period in patients with renal impairment

| Patients with renal impairment \(^*(n = 549)\) | Glycaemic parameters |
|---|---|---|---|
| | FPG (mg/dL) | PPG (mg/dL) | HbA1c (%) |
| Baseline | 177.59 ± 11.67 | 266.37 ± 33.16 | 8.19 ± 0.77 |
| 12 Weeks | 118.88 ± 13.12 | 173.63 ± 32.49 | 7.06 ± 0.84 |
| Difference | – 58.71* | – 92.74* | – 1.13* |

Values in table are presented as the mean ± SD (where appropriate)

\(^*\)Difference is significant at \(p < 0.0001\), paired \(t\) test

### Table 7 Change in the glycaemic parameters from baseline to end of 12-week treatment period in patients according to age category

| Age category \((n = 7593)\) | Glycaemic parameters |
|---|---|---|---|---|
| | FPG (mg/dL) | PPG (mg/dL) | HbA1c (%) |
| < 60 years | 160.37 ± 22.44 | 257.6 ± 47.7 | 8.64 ± 1.12 |
| Baseline | 160.03 ± 21.84 | 169.47 ± 43.19 | 7.64 ± 1.27 |
| 12 Weeks | 116.89 ± 19.24 | 169.47 ± 43.19 | 7.64 ± 1.27 |
| Difference | – 43.48* | – 88.13* | – 1.15* |
| 60–75 years | 160.03 ± 21.84 | 257.6 ± 47.7 | 8.64 ± 1.12 |
| Baseline | 160.03 ± 21.84 | 169.47 ± 43.19 | 7.64 ± 1.27 |
| 12 Weeks | 117.8 ± 22.43 | 169.51 ± 42.43 | 7.56 ± 1.27 |
| Difference | – 42.23* | – 86.82* | – 1.15* |
| > 75 years | 151.01 ± 27.56 | 243.2 ± 44.98 | 8.72 ± 1.26 |
| Baseline | 151.01 ± 27.56 | 243.2 ± 44.98 | 8.72 ± 1.26 |
| 12 Weeks | 109.73 ± 24.12 | 158.15 ± 33.61 | 7.84 ± 1.37 |
| Difference | – 41.28* | – 85.05* | – 0.88* |

Values in table are presented as the mean ± SD (where appropriate)

\(^*\)Difference is significant at \(p < 0.0001\), paired \(t\) test
have not responded well to other antidiabetic drugs such as metformin and SUs. In our study, teneligliptin was preferred as an add-on therapy (96%)—rather than as monotherapy—in patients who had not responded to primary therapy of metformin and/or SUs. This prescription pattern of teneligliptin was also highlighted in a study conducted by Kumar et al. [9], who observed that teneligliptin was preferred as an add-on therapy to metformin and SU. In our patient population, teneligliptin was added to first-line metformin in 40% of patients and to the metformin + SU combination in 34% of patients. The metformin + SU combination remains the mainstay first-line diabetes therapy in India, probably due to its cost effectiveness. However, the natural history of T2DM warrants the use of additional pharmacological agents [10, 11]. Teneligliptin, a relatively new DPP-4I, offers the convenience of once-daily dosing, weight neutrality and a lower risk of hypoglycaemia; consequently, it is commonly used as an add-on to metformin and/or SUs [12].

The effectiveness of teneligliptin in India was first highlighted in the RWE study TREAT-INDIA (n = 4305) conducted by Ghosh et al. [13] in which teneligliptin as a monotherapy and add-on therapy was shown to significantly reduce HbA1c (overall reduction 1.37 ± 1.15% or 15.0 ± 12.6 mmol/mol), FPG (overall reduction 51.29 ± 35.41 mg/dL or 2.85 ± 1.97 mmol/L) and PPG (overall reduction 80.89 ± 54.27 mg/dL or 4.49 ± 3.01 mmol/L). In the present analysis, denoted the TREAT-INDIA 2 study, our patient population was large (n = 10,623) and comprised patients from different regions of country. We also observed that at 12 weeks after initiation of teneligliptin therapy there was a significant decrease from baseline in FPG (43.12 mg/dL or 2.39 mmol/L), PPG (87.73 mg/dL or 4.87 mmol/L) and HbA1c (0.99% or 10.8 mmol/mol). An important difference between the TREAT INDIA 1 and 2 studies is that the TREAT INDIA 2 study also provides insights on the effectiveness of teneligliptin in specific patient populations, such as patients with T2DM with renal impairment and patients with T2DM of different ages. The findings of these above two large-scale RWE studies in the Indian population reflect the effectiveness of teneligliptin. Similar findings were reported in another real-world efficacy study conducted in India by Nashikkar et al. [14]. Changes in HbA1c, FPG and PPG from baseline to end of the study (after 8 weeks of teneligliptin therapy) were –1.22 ± 1.12% or –13.3 ± 12.2 mmol/mol (p = 0.001), –35.8 ± 25.5 mg/dL or –1.99 ± 1.42 mmol/L (p = 0.001) and –60.7 ± 28.6 mg/dL or –3.37 ± 1.59 mmol/L (p = 0.001), respectively. The effectiveness of teneligliptin was also highlighted by Li et al. [15] in a systematic meta-analysis of ten randomized controlled trials (RCTs) in which teneligliptin significantly (p < 0.00001) decreased HbA1c (0.82% or 9.0 mmol/mol), FPG (18.32 mg/dL or 1.02 mmol/L) and PPG (46.94 mg/dL or 2.61 mmol/L). These data lead to the conclusion that teneligliptin effectively improves glycaemic control and is useful in the management of hyperglycaemia in patients with T2DM.

Subgroup analysis of our study population highlights the difference in the reduction in glycemic parameters obtained with teneligliptin as monotherapy and as add-on therapy. HbA1c reduction was 0.70% (7.7 mmol/mol) in patients on teneligliptin monotherapy; in comparison, in patients on combination therapy with teneligliptin as add-on, HbA1c reduction was 0.76% (8.3 mmol/mol) in patients receiving teneligliptin + metformin combination therapy (two drugs), 1.24% (13.6 mmol/mol) in patients receiving metformin + SU combination therapy (three drugs) and 1.04% (11.4 mmol/mol) in patients receiving metformin + SUs + AGIs combination therapy (four drugs). Similar results were seen with the other glycaemic parameters FPG and PPG. These results were also highlighted in the TREAT-INDIA study [13] which reported that HbA1c was reduced by 0.98% (10.7 mmol/mol) with teneligliptin as monotherapy and by 1.11% (12.1 mmol/mol), 1.51% (16.5 mmol/mol), 1.62% (17.7 mmol/mol) and 1.65% (18.0 mmol/mol) when teneligliptin was part of combination therapies consisting of two, three, four and five drugs, respectively. The above results also highlight the importance of adding and continuing teneligliptin as a part of a combination therapy regimen.
Teneligliptin as monotherapy was also effective in this subset of patients in our study (n = 390), significantly (p < 0.001) reducing HbA1c (0.70% or 7.7 mmol/mol), FPG (39.87 mg/dL or 2.21 mmol/L) and PPG (48.30 mg/dL or 2.68 mmol/L). Although, metformin with lifestyle modification is considered to be the initial line of therapy [16], in conditions which prevent the use of metformin, such as patients with renal impairment, the role of metformin is questionable [17] and thus the use of other drugs is justifiable. Kutoha et al. [18] evaluated the use of teneligliptin as first-line therapy in patients newly diagnosed with T2DM. The results of that study showed that teneligliptin significantly reduced HbA1c from 10.34 ± 2.06% (89 ± 22.5 mmol/mol) at baseline to 8.38 ± 2.23% (68 ± 24.4 mmol/mol) at 3 months (p < 0.00001), and FPG from 211.3 ± 68.4 mg/dL (11.73 ± 3.8 mmol/L) at baseline to 167.3 ± 70.2 mg/dL (9.29 ± 3.9 mmol/L) at 3 months (p < 0.0002). Raghavan et al. [19] conducted a 12-week randomized trial in which they compared the effectiveness of teneligliptin with metformin in patients newly diagnosed with T2DM. The results showed that teneligliptin and metformin had similar efficacy in reducing mean HbA1c (0.60% [6.6 mmol/mol] vs. 0.52% [5.7 mmol/mol], respectively), FPG (19.4 mg/dL [1.08 mmol/L] vs. 16.2 mg/dL [0.9 mmol/L], respectively) and PPG (49.8 mg/dL [2.76 mmol/L] vs. 36.8 mg/dL [2.04 mmol/L], respectively). Agarwal et al. [20] reported a significant decrease in mean HbA1c (least squares means difference = −0.31 ± 1.25% [−3.4 ± 13.7 mmol/mol], p = 0.0037) in a 16-week, multicentre, double-blind, placebo-controlled phase 3 trial in India, with a higher percentage (43.6%) of patients achieving the target HbA1c of < 7% with teneligliptin.

When used as an add-on therapy, we found that teneligliptin was added to almost all classes of antidiabetic medications prescribed currently. In our study population, teneligliptin was also added to insulin and other OADs. Insulin therapy is considered to be the most potent hypoglycemic therapy for patients with uncontrolled T2DM, but increasing the insulin dosage is associated with increased risk of hypoglycaemia and weight gain [21–23].

Teneligliptin, when added to insulin therapy, has been shown to decrease the fluctuation in blood glucose levels and increase the proportion of time in the normal glucose range compared to time in hyperglycemia over a 24-h period [24]. Such fluctuations are an important triggering factor for oxidative stress and cardiovascular diseases [25]. Kadowaki et al. [26] in their 16-week RCT reported a significant decrease in blood glucose parameters when teneligliptin was added to insulin. Our results with teneligliptin were similar to those observed in these previous studies.

In our study the combination of teneligliptin and pioglitazone was prescribed in only one patient. AGIs, due to their complementary and different mechanism of action to teneligliptin, increase glucagon-like peptide-1 activity and may provide a valuable option to patients [27–29]. In our study, the therapeutic combination of AGI + teneligliptin was used along with other OADs and achieved a significant decrease in glycemic parameters. Several trials have evaluated the efficacy and safety of gliptins with SUs and have reported a significant improvement in glycemic control [30]. Sodium glucose co-transporter 2 (SGLT2) inhibitors are relatively new class of drugs in the diabetes management algorithm. The combination of teneligliptin with SGLT2 inhibitors, as dual combination therapy, or with other OADs or insulin needs further evaluation. In our study, almost 11% of patients (n = 1118) were given the combination teneligliptin + SGLT2 inhibitor (such as empagliflozin, canagliflozin and dapagliflozin) together with other OADs. Kadowaki et al. [31] reported a significant improvement in the long-term safety and efficacy of canagliflozin as add-on therapy to teneligliptin in Japanese patients, with the results suggesting the effectiveness of this combination in improving HbA1c, FPG and body weight.

We also analyzed the effectiveness of teneligliptin in patients with renal impairment (n = 549). Teneligliptin effectively improved the glycaemic parameters of these patients without worsening the eGFR after 12 weeks of treatment. In a study conducted by Haneda et al. [32], which was an interim report of the post-marketing surveillance over 2 years, long-term treatment with teneligliptin was found to be
effective in reducing the glycaemic parameters and was also well tolerated in patients with any stage of renal impairments from normal to end-stage renal disease. We also analysed the effectiveness of teneligliptin in patients of different ages (three groups: < 60 years, 60–75 years and > 75 years) and found that teneligliptin effectively controlled glycaemic parameters in all age groups. Kadowaki et al. [33] demonstrated that there were no marked or clinically relevant differences in the reductions of FPG or HbA1c at 3 years across these three age subgroups (< 65, ≥ 65 to < 75, or ≥ 75 years).

The biggest strength of this study is the large sample size (>10,000 Indian patients with T2DM), with clinically relevant data collected from a large number of Indian patients representative of the different regions of India. This makes it probably the largest study of real-world data on teneligliptin to date. One of the limitations of this study is its retrospective design, which does not allow determination of a cause-and-effect relationship due to the limited availability of the details of medical records. As this was a single-arm study that focussed on efficacy of teneligliptin, a safety assessment and comparative analysis were not possible.

CONCLUSION

Teneligliptin, a novel DPP-4I, when prescribed either as monotherapy or as an add-on to one or more commonly prescribed antidiabetic agents, significantly improved glycemic parameters. The results of this study suggest that teneligliptin can be considered to be an effective add-on antidiabetic agent in the management of Indian patients with T2DM.

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Data Availability. The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.
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