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Prospective, post-marketing, observational, multi-center, real-world analysis of prescribing patterns of Teneligliptin (INOGLA™) in patients with Type 2 Diabetes Mellitus: GLANCE Study

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Abstract

Background and Objective: Teneligliptin is one of the preferred DPP4 inhibitors as add-on in type 2 diabetes mellitus (T2DM) patients because of established efficacy, safety and low cost. This prospective, observational, multicentric, cross-sectional study was conducted to provide real-world insights on prescribing patterns of INOGLA™ (Teneligliptin 20 mg) in patients with type 2 diabetes mellitus (T2DM) in India.

Methods: Eligible patients prescribed with INOGLA™ at 96 centers between January 2018 and December 2019 were enrolled. Data collection included demographics, anthropometry, diabetes-related history, co-morbidities, antidiabetic and concomitant medications, glycemic control parameters, and creatinine levels. Descriptive statistics were used to summarize quantitative variables using SPSS version 20.0 [IBM CORP, USA].

Results: Of the identified 5276 patients aged ≥18 years, 3126 (59.25%) with available plasma glucose data were included. Mean age was 53.35±11.85 years with male predominance (61.87%). Most patients were either obese (60.58%) or overweight (20.07%). Mean T2DM duration and glycated hemoglobin (HbA1c) were 8.17±6.84 years and 8.37±1.34%, respectively; >90% had uncontrolled HbA1c >7%. About 41.14% had

known co-morbidities; hypertension (32.95%) and dyslipidemia (22.01%) were the most common. More than half (54.25%) had at least one complication; 38.29% had neuropathy and 20.28% had retinopathy. Most (86.92%) were prescribed INOGLA™ 20 mg once-daily dose, followed by 20 mg twice-daily (9.98%). About 15.26% were shifted to INOGLA™ from other DPP-4 inhibitors because of cost or uncontrolled diabetes. With teneligliptin, majority (83.05%) were taking metformin, followed by sulphonylurea (69.73%). Oral antidiabetic agents with teneligliptin ranged from one to six— most preferred was triple combination with metformin + glimepiride.

Conclusion: This real-world GLANCE study shows that INOGLA™ 20 mg once-daily is the most preferred dose in Indian patients with T2DM including elderly, obese, and in co-morbid conditions. Teneligliptin is prescribed with almost all classes of antidiabetic agents for achieving glycemic control, mostly as an add-on therapy to metformin+glimepiride. With substantial burden of microvascular complications, especially neuropathy, this study highlights the need to assess whether teneligliptin therapy can reduce the burden of diabetes-related complications in our population.

Keywords: Teneligliptin, DPP-4 inhibitors, Diabetes Mellitus.

Introduction

Diabetes prevalence has been rising, affecting around 9.3% (463 million adults, 20-79 years) people globally in 2019, and is estimated to affect 10.9% (700 million) by 2045. Low- and middle-income countries contribute to nearly 75% of the disease burden. Asia is at the epicenter of this epidemic owing to a phenotype characterized by young age of onset, predisposition to beta-cell failure and visceral adiposity.2 India is second most leading country after china in diabetes burden with 77 million individuals with diabetes in 2019, projecting to reach 134.2 million by 2045.2 nearly 1 in 6 adults with diabetes in the world hails from india. ,type 2 diabetes mellitus (t2dm) accounts for over 90% of all forms of diabetes, caused by either a disturbed insulin secretion or a disturbed insulin effect or both leading to chronic hyperglycemia.1, delayed diagnosis and failure to screen for early-stage complications lead to enhanced risk for development of serious complications, morbidity and mortality. T2dm is often diagnosed only once complications develops— namely microvascular (neuropathy, nephropathy, and retinopathy) and macrovascular (cardiovascular, peripheral vascular, and cerebrovascular disease). Suboptimal glycemic control and impaired insulin sensitivity increases the risk of these complications. , , a study conducted in 10 developing countries reported a poor glycemic condition with a mean ± standard deviation (sd) baseline hba1c of 9.7 ± 1.8% associated with microvascular complications in about 87.9% of study population. Empirical evidence from other studies also demonstrate independent associations of micro- and macrovascular complications with reduced quality of life, an enhanced risk of major adverse cardiovascular events and mortality. Progressive decline in β-cell function limits the long-term use of metformin monotherapy. Hence, the guidelines recommend timely addition of a second agent post failure of metformin monotherapy for achieving and maintaining optimum glycemic control. dipeptidyl peptidase-4 inhibitors (dpp-4i) are a promising class of oads, which inhibit the endogenous glucagon-like peptide-1 (glp-1) metabolism. It increase glp-1 levels in the physiological range and thereby regulates blood glucose levels post meal. Dpp-4i have shown to reduce complications of t2dm caused by glycemic variability

as compared to other class of oads. Vildagliptin, sitagliptin, linagliptin, saxagliptin, gemigliptin and teneligliptin are approved as adjuncts to diet and exercise to improve glycemic control in adults with t2dm. Teneligliptin, a novel dpp-4i, has a unique j structure characterized by five consecutive rings; the interaction occurs between the phenyl ring on the pyrazole of teneligliptin and the s2 extensive subsite of dpp-4 enzyme. These unique properties with 24 hours plasma half-life produce a potent, selective and long-lasting glucose-lowering effect. Teneligliptin controls the decomposition of glp-1 by inhibiting dpp-4 activity and thereby increasing blood concentration of active form glp-1. Teneligliptin has been extensively evaluated for efficacy, safety and tolerability in various clinical studies. Long-term treatment with teneligliptin was generally well-tolerated in patients with any stage of renal impairment, including end-stage renal disease on dialysis. Teneligliptin was well-tolerated by subjects with mild to moderate hepatic impairment and no dose adjustment is required in these patients. The treat-india study demonstrated significant hba1c reduction with teneligliptin (-1.0 ± 0.5%) when used as add-on to metformin (-1.1 ± 0.8%) or add-on to metformin plus sulfonylurea combination (-1.46 ± 1.33%). The glance study aimed to provide real-world insights on prescribing patterns of inogla™ (teneligliptin 20 mg) in indian patients with t2dm. The ultimate goal is to improve patient care and clinical outcomes in india by collecting reliable, real-world clinical data on prescribing practice, disease characteristics and complications to understand current gaps in the contemporary clinical management of t2dm.

Methodology

Study design and assessment: This prospective, observational, multicentric, cross-sectional post-marketing study was conducted at 96 centers across India between January 2018 and December 2019 with a total sample of 5276 subjects. The primary objective was to understand the prescribing patterns of INOGLA™ in patients with T2DM from routine clinical practice. After obtaining approval from the Institutional Review Board of the participating centres, the study was conducted in compliance with the protocol and all applicable regulatory guidelines. Written informed consent was obtained from all participating patients prior to study procedures. Male and female patients with T2DM (with no specific age bar) who were prescribed with INOGLA™ as part of standard clinical care were included in the study and patients less than 18 year , pregnant women and type 1 diabetics were excluded from the study.

Data collection included demographics, anthropometry, personal and family history, co-morbid conditions, ongoing anti-diabetic therapy, concomitant medications, and laboratory results (HbA1c, fasting blood glucose [FBG], post-prandial blood glucose [PPBG] and creatinine levels). All study related data were recorded on a structured Case Record Form.

Statistical analyses

Demographic data such as age, gender, weight, body mass index (BMI) were summarized using descriptive statistics. Summary statistics for quantitative variables included the number of observations (n), arithmetic mean, SD. Statistical analyses were performed using Statistical and Analytical Software (SPSS version 20.0 [IBM CORP, USA]).

Results

Demographic and Clinical Profile: A total of 5276 patients aged ≥18 years were identified, of which 3126 (59.25%) patients' data had complete information on plasma glucose levels. Hence, the prescribing pattern of

INGOLA™ was analysed in this subset of 3126 patients. Table 1 presents the demographic and clinical characteristics of the study population. Majority (85%) of the patients were >40 years (41-60 years [56.94%], 61-80 years [26.58%], >81 years [1.5%]). The mean ± SD age of patients was 53.35 ± 11.85 years, with male predominance (1934, 61.87%). The mean ± SD (95% interval) weight and BMI at baseline were 70.26 ± 10.98 (23.00, 150.00) kgs and 26.32 ± 4.06 (19.58, 35.50) kg/m^2, respectively. Most (1669, 60.58%) patients were obese (BMI ≥25 kg/m^2), followed by overweight (553, 20.07%) with BMI in the range 23-24.99 kg/m^2. The mean ± SD (range) duration of diabetes was 8.17 ± 6.84 (0.08-40.08) years in 92.16% of patients with existing history of diabetes; 245 (7.84%) patients were newly diagnosed. More than one-fourth (827, 28.71%) of patients had 1st degree relatives with known history of T2DM.

Figure 1a provides the prevalence of comorbid conditions in the patient population (reported in >5 patients). More than one-thirds (1286, 41.14%) of patients had known co-morbidities; hypertension was the most (1030, 32.95%) common, followed by dyslipidemia in 688 (22.01%) patients; less than 10% of patients had coronary artery disease (CAD) (259, 8.29%), hypothyroidism (47, 1.47%) and congestive heart failure (CHF) (24, 0.77%).

Microvascular and macrovascular complications: About 54.25% (1696) of the patients had at least one complication; the frequency of microvascular complication was higher for neuropathy (1197, 38.29%), followed by retinopathy (634, 20.28%), chronic kidney disease (172, 5.5%). The mean ± SD (range) serum creatinine level and eGFR were 2.31 ± 1.59 (0.60-6.60) mg/dl and 43.67 ± 17.78 (20-67) ml/min/1.73 m^2, respectively. Diabetic foot was reported as complication in 9 patients and as a comorbid illness in 3 patients. Peripheral vascular disease was observed in 315 (10.27%) patients; complications were present but not specified in about 10% of patients. Other complications listed in >5 patients are shown in Figure 1b.

Glycemic control and antidiabetic therapy: The mean ± SD (range) FBG and PPBG values were 171.85 ± 38.88 (76.0-548.0) mg/dl and 272.47 ± 69.55 (85.0-563.0) mg/dL, respectively. The mean ± SD (range) HbA1c was 8.37 ± 1.34 (0.70-16.20)% with a median of 8.20%. Nearly 2834 (90.66%) patients had uncontrolled HbA1c >7%. Of patients with uncontrolled diabetes, 1122 (39.59%) had HbA1c between 7% and 8%, 1422 (50.18%) had HbA1c between 8% and 10%, while 290 (10.23%) had HbA1c >10%. Patients with uncontrolled HbA1c had 1551 (54.73%) cases of obesity and 980 (34.58%) cases of hypertension compared with patients having controlled HbA1c (obesity: 118 [40.41%], hypertension: 50 [17.12%]).

Table 2 provides descriptive statistics of various parameters like age, BMI, plasma glucose and HbA1c per INOGLA™ dose levels. Of 3126 patients, most (2717, 86.92%) patients were on 20 mg once a day (OD) dose, followed by 20 mg twice a day (BD) dose (312, 9.98%). However, due to imbalance of patient numbers across groups, the inferential statistical tests were not applied for these parameters. A total of 477 (15.26%) patients were shifted to INOGLA™ from other DPP-4i. About 47 (32.19%) and 99 (67.81%) patients shifted from sitagliptin and vildagliptin, respectively to INOGLA™ (Figure 2a and 2b). The most common reasons for these shifts were cost (from sitagliptin [10, 21.27%], from vildagliptin [26, 26.3%]) and 'DM not controlled' (from sitagliptin [6, 12.76%],

from vildagliptin [6, 6.06%)]) (Figure 2a and 2b). The reasons were unknown in about half (from sitagliptin [22, 46.8%], from vildagliptin [44, 44.4%]) of the patients.

With teneligliptin, majority (2596, 83.05%) of the patients were on metformin, followed by sulphonylurea (glimepiride [1824, 58.35%], gliclazide [167, 5.34%], glipizide [127, 4.06%] and glibenclamide [62, 1.98%]) (Table 3 and Figure 3). Among 738 patients on alpha-glucosidase inhibitors, 679 (21.72%) and 59 (1.89%) were on voglibose and acarbose, respectively. Of 280 patients on sodium-glucose co-transporter-2 (SGLT-2) inhibitors, 109 (3.49%) were on dapagliflozin, followed by 94 (3.01%) on empagliflozin, and 77 (2.46%) on canagliflozin. About 78 patients were on GLP-1 agonist class of drugs (exenatide: 42, 1.34%; liraglutide: 31, 0.99% and dulaglutide: 5, 0.16%). There were 419 (13.4%) and 25 (0.8%) patients on pioglitazone and saroglitazar, respectively. Little more than 10% patients were on insulin (Premixed: 256, 8.19%; Basal: 88, 2.82% and Rapid: 38, 1.22%).

The concomitant antidiabetic drugs were prescribed mostly with 20 mg OD of INOGLA^{TM}, in more than 80% of the patients. There were 10% or more patients with metformin, glimepiride and gliclazide as concomitant drugs with 20 mg BD of INOGLA^{TM}. The combinations of other dosing patterns of INOGLA^{TM} and concomitant medications were observed in less than 10% of the patients. Likewise, insulin usage was predominant with 20 mg OD of INOGLA^{TM} (Table 3).

The OAD combinations with teneligliptin ranged from one to six (Table 4). Teneligliptin mono therapy was being prescribed for only 213 (6.98%) patients. With teneligliptin, 404 (13.24%) and 142 (4.65%) patients were taking metformin and glimepiride, respectively. More than two-thirds (1274, 41.75%) were on 2 OADs with teneligliptin; 925 (30.32%) were taking metformin+glimepiride, followed by 105 (3.44%) with metformin+voglibose, 81 (2.65%) with metformin+gliclazide, and 31 (1.02%) with metformin+pioglitazone. About one-fourth (774, 25.36%) of patients were being treated with different combinations of 3 OADs with teneligliptin; 303 (9.93%) patients were on metformin+glimepiride+voglibose, followed by 173 (5.67%) on metformin+glimepiride+pioglitazone, 41 (1.34%) on metformin+glimepiride+empagliflozin, 37 (1.21%) on metformin+glipizide+pioglitazone and 36 (1.18%) on metformin+voglibose+pioglitazone. About 105 (3.44%) patients were taking 4 OADs along with teneligliptin;

metformin+glimepiride+voglibose+pioglitazone was the most common (41, 1.34%). The combinations of 5 and 6 OADs along with teneligliptin were observed in 76 and 1 patient, respectively.

Discussion

This nationally representative cross-sectional study assessed the prescribing patterns of INOGLATM in 3126 patients with T2DM from routine clinical practice for a period of 2 years; the study also explored the disease characteristics, glycemic control and reasons for shifts to teneligliptin therapy. Most physicians (>85%) preferred 20 mg OD dose of INOGLATM with dual or multiple antidiabetic drugs. Metformin (83.05%) and sulphonylurea (69.73%) remain as the mainstay first-line diabetes therapy in India, probably due to its cost effectiveness to which teneligliptin was added to achieve glycemic control. The international and national guidelines recommend addition of any one of the preferred six treatment options with metformin based on drug-specific effects and patient factors: sulfonylurea, thiazolidinedione, DPP-4i, SGLT2

inhibitor, GLP-1 RA, or basal insulin if the HbA1c target is not achieved after approximately 3 months of metformin therapy. , , Teneligliptin was added to first-line metformin in about 13% and to the metformin+SU combination in 30% of our study population.INOGLATM was prescribed in the elderly patients, which consisted about one-fourth (28.1%) of the entire study population. Because of a lower risk of hypoglycemia, DPP-4i are preferred for glycemic control in the elderly T2DM patients as altered pharmacokinetic profile is associated with aging and polypharmacy. A pooled analysis of two phase III trials has shown that teneligliptin as monotherapy or combination therapy has similar adverse event (AE) profile with lesser risk of hypoglycemia as compared to sulfonylurea for as long as 52 weeks. , Recently, a 3-year post-marketing surveillance (PMS) from Japan reported no additional safety concerns in the elderly population except for those already known for teneligliptin; improvements in glycemic control observed within 6 months of treatment initiation were maintained over the course of 3 years. In the interim analyses of this PMS (>10000 patients), stratified by age (<65 and ≥ 65 years), no elevation in the incidence of hypoglycemia was observed in patients aged <65 years versus those aged ≥ 65 years, even when teneligliptin was used as an adjunct to insulin. The involvement of multiple metabolic enzymes, together with multiple elimination pathways, makes teneligliptin less susceptible to age-related pharmacokinetic changes and drug–drug interactions.Our study results also confirm the real-world burden of uncontrolled diabetes in India with a mean HbA1c of 8.37 ± 1.34% for whom teneligliptin was a preferred choice as an add-on to the existing anti-diabetic therapy. We found longer duration of diabetes and obesity to be predominant in the study population. A retrospective study from China reported >4 years of diabetes duration to be associated with higher odds (OR=5.98, 95% CI: 4.09, 8.75) of poor glycemic control. Obesity and hypertension are well-established comorbidities for T2DM; a meta-analyses of observational studies from India showed a significant association between obesity and T2DM (pooled OR = 1.14, 95%CI: 1.04-1.24). More than 80% of the study patients were either obese or overweight. Most of the studies in past reported neutral impact of DPP-4i on the BMI. Recently, an age-adjusted analysis of a retrospective study from India reported a significant reduction in BMI before and after higher dose teneligliptin addition to ongoing monotherapy.In the OAD combinations with teneligliptin, triple combination of 2 OADs plus teneligliptin was the most common. INOGLATM was prescribed along with almost all classes of antidiabetic agents majority were taking metformin (>80%) and glimepiride (~60%). DPP-4i therapy with metformin lowers the risk of severe hypoglycemia, cardiovascular events, and all-cause mortality when compared to metformin plus sulphonylurea. One-fifth (21.72%) of patients were on voglibose and 13.4% on pioglitazone. Less than 10% patients were taking SGLT-2 inhibitors, GLP-1 agonist class of drugs and insulin. These concomitant antidiabetic drugs and insulin use were predominant with 20 mg OD dose of INOGLATM, in more than 80% of patients. About 10% of patients taking metformin, glimepiride and gliclazide were prescribed with 20 mg BD dose of INOGLATM.The study population had a substantial burden of co-morbidities in >40%─ hypertension, dyslipidemia, CAD, hypothyroidism and CHF were most frequently reported. A major proportion of diabetic patients are often diagnosed with hypertension, twice as likely to

have hypertension compared with individuals without diabetes. DPP-4i have recently shown to enhance nitric oxide release in hypertensive or diabetic models. An observational study with teneligliptin reported statistically significant decreases in systolic and diastolic blood pressure at 3 and 6 months from baseline (all p<0.001). In diabetic patients with dyslipidemia, teneligliptin add-on treatment with atorvastatin reduced glycemic and lipid parameters as well as improved adiponectin levels as compared with conventional-therapy. A statistically significant decrease in apoB-48 was observed during fasting and after a meal post 6-month treatment with teneligliptin. These results suggest that teneligliptin may be beneficial for treating postprandial hyperlipidemia in patients with T2DM.As a well-known consequence, we observed a significant burden of microvascular complications. More than half of the population (54.25%) had any complication─ predominantly neuropathy (38.29%), followed by retinopathy (20.28%) and nephropathy (5.5%). Studies from India report a varied prevalence of neuropathy (14.7%-29.2%), retinopathy (10.4%-32.5%) and nephropathy (6.2%-30.2%) across healthcare facilities.12, , , A meta-analysis from randomized controlled trials over 5 years reported that intensive glucose control compared with less intensive glucose control reduced relative risk by 20% for microvascular nephropathy (hazard ratio [HR] 0.80, p < 0.0001) and by 13% for retinopathy (0.87, p = 0.04), but not for neuropathy (0.98, p = 0.68). A prospective study revealed that risks of all-cause and cardiovascular disease (CVD) mortality were significantly higher in patients with diabetic kidney disease (DKD) and diabetic retinopathy (DR) compared with those with no DR and DKD (HR of all-cause and CVD mortality:1.89 [95% confidence interval {CI}, 1.40-2.57] and 2.26 [95% CI, 1.42-3.61], respectively, for DKD alone and 1.38 [95% CI, 1.03-1.86] and 1.64 [95% CI,1.06-2.56], respectively, for DR alone). Use of DPP-4i improves long-term survival in diabetic patients after first acute myocardial infarction, regardless of gender and reduces risk of heart failure hospitalization compared to GLP-1 agonists. , Teneligliptin has also shown an anti-atherothrombotic effect that may be favorable in the primary prevention of CVD in patients with T2DM on hemodialysis. To determine whether teneligliptin improves LV diastolic dysfunction and whether teneligliptin prevents progressive worsening of LV diastolic function in T2DM patients (n=1,000), an open-label, marker-stratified, randomized multicenter TOPLEVEL study is ongoing. Chronic kidney disease was reported in about 5.5% of the study patients with a mean ± SD eGFR below 60 ml/min/1.73 m2. Because of its multiple elimination pathways, dose adjustments are not needed for teneligliptin in patients with hepatic and renal impairment. , Significant and sustained improvements in glycemic control was reported in Asian Indian patients of T2DM with early DKD who were treated with teneligliptin, 20 mg OD for 24 weeks.Many patients shifted from prototype DPP-4i, sitagliptin or vildagliptin to INOGLATM for want of reducing cost (26.3%) or achieving tight glycemic control (6.06%); reasons were unknown in about half of the patients. Studies have demonstrated non-inferiority of switching agents within the same class as a treatment option. In a switching study in patients with inadequate glycemic control, switch from other DPP-4i to teneligliptin lowered HbA1c levels significantly from baseline to week 12. Similar significant glycemic benefits (FBG, PPBG, and HbA1c) were observed in an Indian study wherein switch to teneligliptin from other gliptins was

made in T2DM patients uncontrolled with OADs.With increasing prevalence of T2DM in the Indian subcontinent, optimum pharmacotherapy is necessary to delay micro- and macrovascular complications. As recommended by clinical practice guidelines, prescription of combination therapy with metformin and newer OHAs including gliptins has increased over the years. However, in India the stepwise approach of sequential addition of other OHAs to metformin monotherapy is often delayed.8 Therapeutic inertia, gaps in disease monitoring, patient resistance to lifestyle measures and poor drug adherence act as crucial challenges causing poor glycemic control, culminating in a cascade of complications. , A meta-analysis demonstrated that early combination therapy with metformin compared with metformin alone leads to increase in the number of patients achieving HbA1c goal of <7% (relative risk 1.40). The multitude of second-line therapy options often makes the clinical decision-making process complex. In the past few years, incretin-based therapies such as DPP-4i, GLP-1 agonists and SGLT2 inhibitors have emerged as preferred drugs due of their efficacy and acceptable safety profile. As an affordable and efficacious alternative gliptin, teneligliptin has shown to reduce the average pharmacotherapy cost by about 80% in India when compared to other DPP-4i. They have lower risk for hypoglycemia through unique glucagon dynamics. Unlike sitagliptin, teneligliptin does not require dose adjustment/reduction in patients with renal (including patients on dialysis) and hepatic impairment because of its dual mode of excretion, providing a notable advantage in these patients.Limitations of this study include its cross-sectional design (single visit with no follow-up data) because of which efficacy and safety of INOGLATM therapy could not be determined. Also a causal relationship between glycemic control over the course of INOGLATM treatment and development of microvascular complications could not be established. Another challenge was availability of limited data on macrovascular complications, which made it difficult to differentiate from baseline comorbidities. Despite these limitations, our study highlights the prescribing practices from routine clinical practice wherein INOGLATM 20 mg OD dose is preferred as an add-on therapy with all classes of antidiabetic agents for achieving glycemic control in elderly, obese, and in co-morbid conditions. However, further research is required to ascertain if teneligliptin therapy can reduce the substantial burden of micro- and macrovascular complications in our population in the long-term.

Conclusion

To conclude, results of this real-world GLANCE study show that INOGLA^{TM} 20 mg OD is the most preferred dose in Indian patients with T2DM including elderly, obese, and in co-morbid conditions. There is a considerable burden of uncontrolled diabetes having a poor glycemic control (mean HbA1c ≥7%) for whom teneligliptin is prescribed with almost all classes of antidiabetic agents for achieving glycemic control, mostly as an add-on therapy to metformin+glimepiride. With substantial burden of microvascular complications, especially neuropathy, this study highlights the need to assess whether teneligliptin therapy can maintain the recommended glycemic control, thereby reducing the burden of diabetes-related complications. Enhanced awareness among patients and providers, curbing clinical inertia, individualized patient-centered therapy with timely addition of a second anti-diabetic agent, together with optimal care of comorbidities like hypertension and dyslipidemia remain the mainstay of reaching glycemic targets.

Legend Tables

Table 1: Demographic and disease characteristics of study population (N=3126)

Parameter	N=3126	Median	Range
Age (years), mean (SD)	53.35 ± 11.85	53.00	19.0, 98.0
≤ 40 years, n (%)	463 (14.8)	-	-
41-60 years, n (%)	1780 (56.9)	-	-
61-80 years, n (%)	831 (26.6)	-	-
≥ 81 years, n (%)	47 (1.5)	-	-
Unknown, n (%)	5 (0.16)	-	-
Gender, n (%)			
Female	1155 (36.9)	-	-
Male	1934 (61.9)	-	-
Unknown	37 (1.2)	-	-
Weight (kg), mean (SD)	70.26 ± 10.98	69.0	23.0, 150.0
BMI* (kg/m²), mean (SD)	26.32 ± 4.06	25.91	19.58, 35.5
Underweight, n (%)	25 (0.9)	-	-
Normal, n (%)	508 (18.4)	-	-
Over-weight, n (%)	553 (20.0)	-	-
Obese, n (%)	1669 (60.6)	-	-
Unknown	371 (11.86)	-	-
Duration of T2DM, mean (SD)	8.17 ± 6.84		-
Recently diagnosed, n (%)	245 (7.84)	-	-
Previously diagnosed, n (%)	2881 (92.16)	6.67	0.08, 40.08
Family history of T2DM (N=2881), n (%)			
First-degree relatives	827 (28.7)	-	-
None	1265 (43.9)	-	-
Unknown	789 (27.4)	-	-
Laboratory results, mean (SD)			
FBG (mg/dL)	171.85 ± 38.88	171.00	76.00, 548.00
PPBG (mg/dL)	272.47 ± 69.55	268.00	85.00, 563.00
HbA1c (%)	8.37 ±1.34	8.20	0.70, 16.20
Chronic kidney disease, mean (SD)			
Serum creatinine, mg/dL (n=22)	2.31 (1.59)	1.80	0.60, 6.60
eGFR, mL/min/1.73 m2 (n=6)	43.67 (17.78)	44.00	20.00, 67.00
INOGLA™ dose, n (%)			

Parameter	N=3126	Median	Range
20 mg OD	2717 (86.9)	-	-
20 mg BD	312 (10)	-	-
20 mg OD and 20 mg BD	9 (0.3)	-	-
40 mg OD	13 (0.4)	-	-
Dose not mentioned	75 (2.4)	-	-

BD: twice a day; BMI: body mass index; eGFR: estimated glomerular filtration rate; FBG: fasting blood glucose; HbA1c: glycosylated hemoglobin; OD: once a day; PPBG: post-prandial blood glucose; SD: Standard deviation

Percentages are calculated based on total number of subjects in the respective treatment arm

n=Number of subjects in respective categories; N=Total number of subjects analysed

Percentages are based on the overall counts

*BMI categories (kg/m2): Underweight < 18.5; Normal: 18.5-22.9; Overweight: 23.0-24.9; Obesity: > 25

Table 2: Demographic and glycemic parameters as per INOGLA™ dosages (N=3126)

Parameter	INOGLA™ (mean ± SD)				
	20 mg OD (n=2717)	20 mg BD (n=312)	20 mg OD & 20 mg BD (n=9)	40 mg OD (n=13)	Dose not mentioned (n=75)
Age (years)	53.91 ± 12.03	54.74 ± 11.16	54.11 ± 8.88	64.00 ± 9.50	44.92 ± 13.75
BMI (kg/m^2)	26.42 ± 4.10	25.16 ± 3.93	27.54 ± 1.96	26.02 ± 3.04	26.59 ± 4.47
FBG (mg/dl)	172.10 ± 36.84	182.56 ± 39.58	201.89 ± 42.93	176.62 ± 36.41	128.27 ± 29.74
PPBG (mg/dl)	269.88 ± 69.26	295.57 ± 70.83	320.67 ± 53.67	264.23 ± 54.59	250.85 ± 41.81
HbA1C (%)	8.36 ± 1.33	8.29 ± 1.47	9.57 ± 1.87	9.63 ± 1.12	8.61 ± 0.73

BD: twice a day; BMI: body mass index; FBG: fasting blood glucose; HbA1c: glycosylated hemoglobin; OD: once a day; PPBG: post-prandial blood glucose; SD: Standard deviation

Table 3: Concomitant anti-diabetic therapy as per INOGLA™ dosages (N=3126)

Class of drugs	Concomitant antidiabetic drug	INOGLA™ Dose, n (%)					Total (%)
		20 mg OD	20 mg BD	20 mg OD & 20 mg BD	40 mg OD	No dose	
BIGUANIDES	Metformin	2292 (88.29)	269 (10.36)	8 (0.31)	7 (0.27)	20 (0.77)	2596 (83.05)
SULPHONYLUREA	Glimepiride	1568 (85.96)	232 (12.72)	5 (0.27)	5 (0.27)	14 (0.77)	1824 (58.35)

	Gliclazide	140 (83.83)	20 (11.98)	2 (1.2)	4 (2.4)	1 (0.6)	167 (5.34)
	Glipizide	121 (95.28)	4 (3.15)	0 (0)	0 (0)	2 (1.57)	127 (4.06)
	Glibenclamide	56 (90.32)	5 (8.06)	0 (0)	0 (0)	1 (1.61)	62 (1.98)
αGLUCOSIDASE INHIBITOR	Voglibose	618 (91.02)	54 (7.95)	1 (0.15)	2 (0.29)	4 (0.59)	679 (21.72)
	Acarbose	56 (94.92)	3 (5.08)	0 (0)	0 (0)	0 (0)	59 (1.89)
	Dapagliflozin	93 (85.32)	9 (8.26)	0 (0)	4 (3.67)	3 (2.75)	109 (3.49)
SGLT-2 INHIBITOR	Canagliflozin	71 (92.21)	2 (2.6)	1 (1.3)	1 (1.3)	2 (2.6)	77 (2.46)
	Empagliflozin	88 (93.62)	5 (5.32)	0 (0)	0 (0)	1 (1.06)	94 (3.01)
GLP-1 AGONIST	Exenatide	41 (97.62)	1 (2.38)	0 (0)	0 (0)	0 (0)	42 (1.34)
	Liraglutide	29 (93.55)	2 (6.45)	0 (0)	0 (0)	0 (0)	31 (0.99)
	Dulaglutide	5 (100)	0 (0)	0 (0)	0 (0)	0 (0)	5 (0.16)
PPAR AGONIST	Pioglitazone	386 (92.12)	29 (6.92)	0 (0)	3 (0.72)	1 (0.24)	419 (13.4)
	Saroglitazar	22 (88)	0 (0)	0 (0)	2 (8)	1 (4)	25 (0.8)
MEGLITINIDES	Repaglinide	8 (100)	0 (0)	0 (0)	0 (0)	0 (0)	8 (0.26)
	Nateglinide	1 (100)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0.03)
PREMIXED INSULIN		234 (91.41)	13 (5.08)	0 (0)	8 (3.13)	1 (0.39)	256 (8.19)
BASAL INSULIN		76 (86.36)	7 (7.95)	1 (1.14)	4 (4.55)	0 (0)	88 (2.82)
RAPID ACTING INSULIN		32 (84.21)	3 (7.89)	0 (0)	2 (5.26)	1 (2.63)	38 (1.22)
No medication prescribed		170 (69.11)	18 (7.32)	1 (0.41)	2 (0.81)	55 (22.3)	246 (7.87)

BD: twice a day; BMI: body mass index; FBG: fasting blood glucose; GLP: Glucagon-like peptide; HbA1c: glycosylated hemoglobin; OD: once a day; PPBG: post-prandial blood glucose; PPAR: Peroxisome proliferator-activated receptor; SD: Standard deviation; SGLT-2: Sodium-glucose co-transporter-2

Table 4: Combination therapy with teneligliptin (N=3051)

Combinations	n	%
Teneligliptin without any other OADs (monotherapy)	213	6.98
Teneligliptin with one OAD (dual)	617	20.12
Metformin	404	13.24
Glimepiride	142	4.65
Teneligliptin with 2 OADs (triple)	1274	41.75
Metformin+Glimepiride	925	30.32
Metformin+Voglibose	105	3.44
Metformin+Gliclazide	81	2.65
Metformin+Pioglitazone	31	1.02
Teneligliptin with of 3 OADs	774	25.36
Metformin+Glimepiride+Voglibose	303	9.93
Metformin+Glimepiride+Pioglitazone	173	5.67

Metformin+Glimepiride+Empagliflozin	41	1.34
Metformin+Glipizide+Pioglitazone	37	1.21
Metformin+Voglibose+Pioglitazone	36	1.18
Teneligliptin with 4 OADs	105	3.44
Metformin+Glimepiride+Voglibose+Pioglitazone	41	1.34
Teneligliptin with 5 OADs	76	2.49

Table includes data of >1% of patients prescribed combination therapy with teneligliptin

*01 patient was on teneligliptin with 6 OADs

OAD: Oral anti-diabetic drug

Figure 1: Prevalence of comorbid illnesses and complications in study population (N=3126)

Figure 1a: Prevalence of comorbid illness

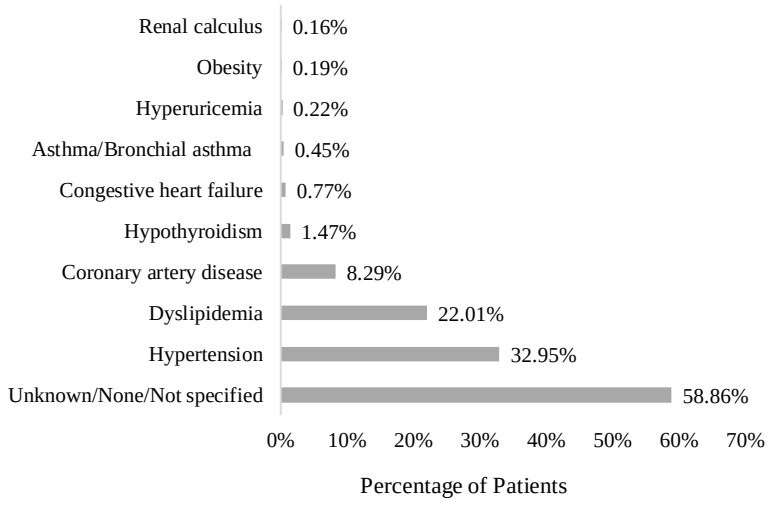


Figure 1b: Prevalence of microvascular and macrovascular complications

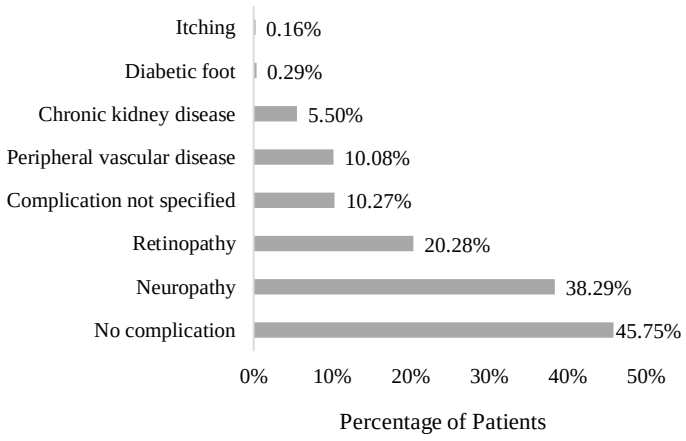
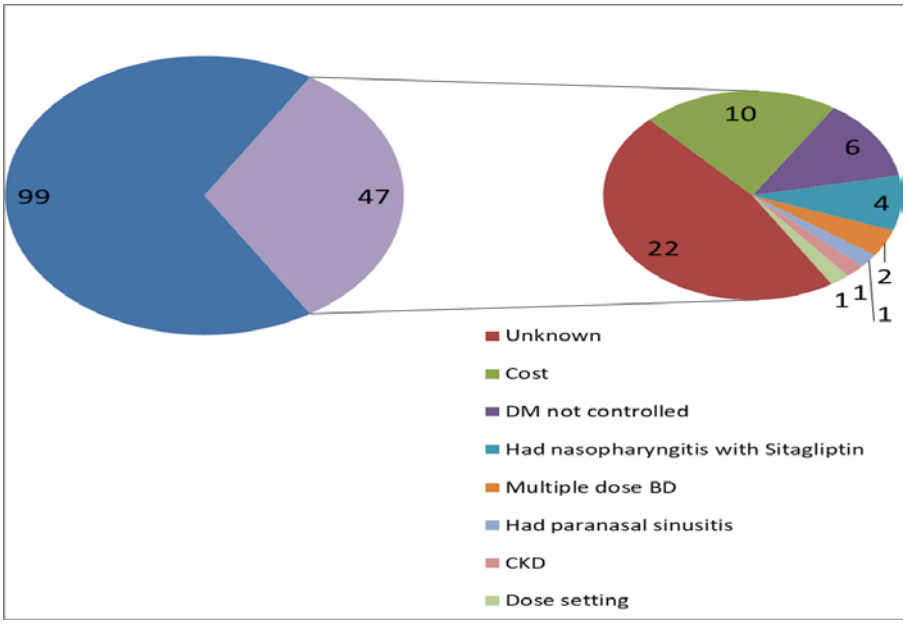


Figure includes data of >5 patients with a comorbid illness and complication

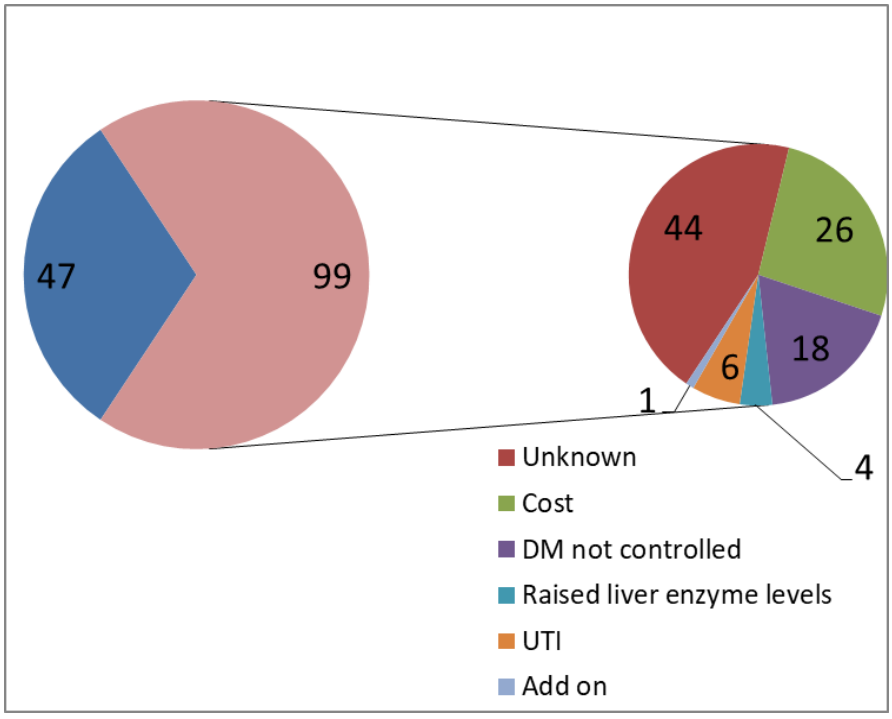
Comorbid illness reported in <5 and >3 patients: Anemia (04), Cerebrovascular accident (03), Gastroesophageal reflux disease (03) and Diabetic foot (03) Complications reported in <5 and >3 patients: Fatty liver (04), Thyroid disorder (03), Erectile dysfunction (03), Asthma (03).

Figure 2a: Shift from Sitagliptin to INOGLA™ and reasons for shifts (N=47)



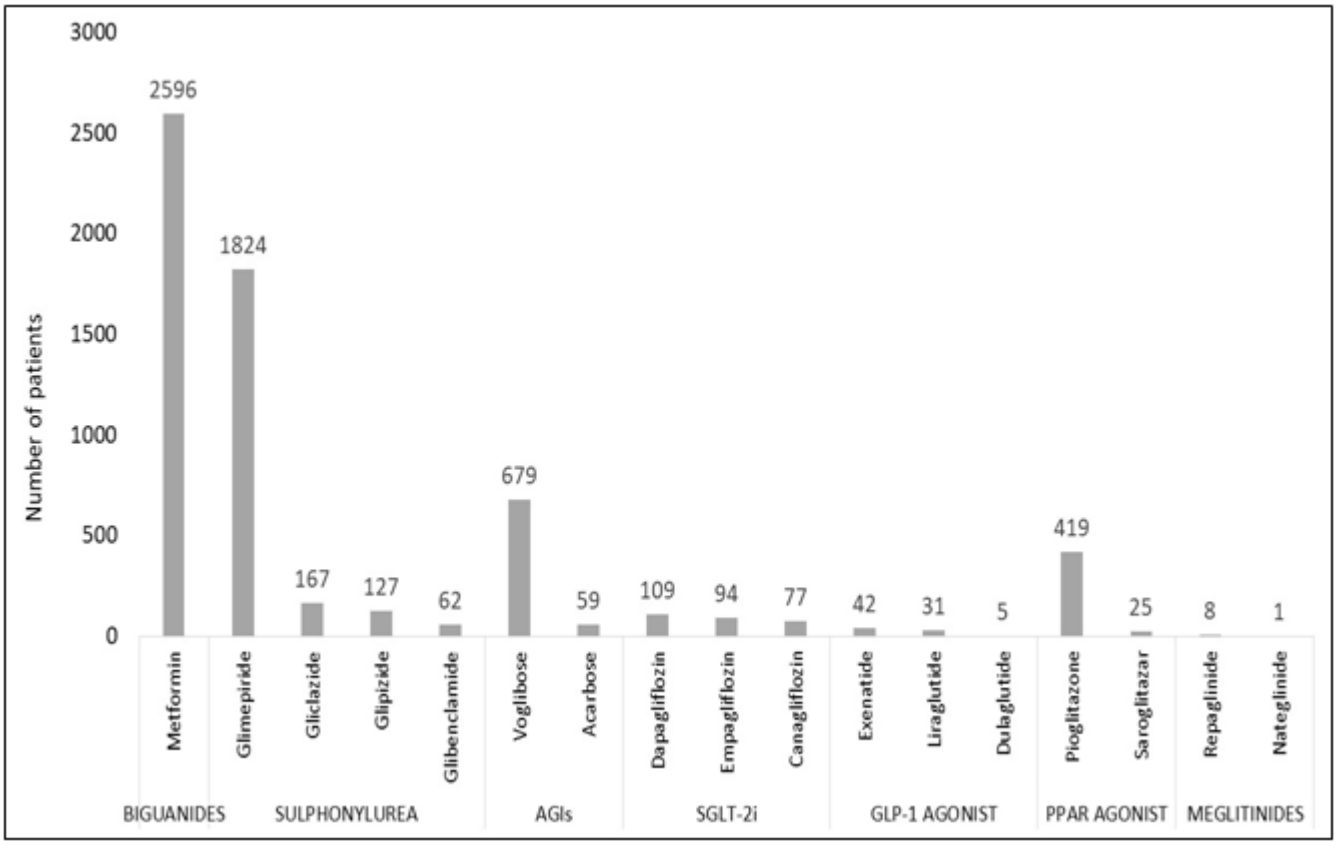
BD: twice a day; CKD: Chronic kidney disease; DM: Diabetes mellitus; UTI: urinary tract infection

Figure 2b: Shift from Vildagliptin to INOGLA™ and reasons for shifts (N=99)



CKD: Chronic kidney disease; DM: Diabetes mellitus; UTI: urinary tract infection

Figure 3: Concomitant anti-diabetic therapy with INOGLA™ (N=3126)



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