

Type 2 Diabetes and comorbidities DISCOVERing in Real World (From The DISCOVER Program*) : Algeria Baseline Data.

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ABSTRACT

La prise en charge des patients atteints de diabète de type 2 reste complexe et les données de la vraie vie restent rares.

OBJECTIFS

Décrire les caractéristiques à l'inclusion et le traitement des patients atteints de diabète de type 2 en Algérie en début de traitement hypcholestérolémiant de deuxième intention dans le cadre du programme mondial d'étude DISCOVER.

MÉTHODES

Le programme d'études observationnelle DISCOVER en cours (NCT02322762) et J-DISCOVER au Japon (NCT02226822) a inclus plus de 15 000 patients dans 38 pays, dont l'Algérie à travers six continents. La collecte de données concerne la base de référence (l'initiation d'un traitement antidiabétique de deuxième intention), six mois et chaque année pour une période de suivi de trois ans. Les principales caractéristiques enregistrées sont les paramètres de santé et les indicateurs de la prise en charge du diabète de type 2.

RÉSULTATS

293 patients algériens ont été inclus. Les spécialités des principaux investigateurs sont la médecine interne (50%), les endocrinologues-diabétologues (28,6%) et les médecins généralistes / médecins de famille (21,4%). L'âge moyen était de $55,3 \pm 10,7$ ans avec un sex-ratio M / F de 0,95. La durée moyenne du diabète était de $5,85 \pm 4,78$ ans. L'indice de masse corporelle (IMC) moyen était de $29,1 \pm 4,6$ kg / m² et l'HbA1c moyen de $8,3 \pm 1,6\%$. La metformine était le traitement de première intention chez 77,5% des patients et les raisons des modifications du traitement étaient dominées par le manque d'efficacité. Dictée par la disponibilité des classes de médicaments, le traitement de première intention a été dominé par la metformine et le traitement de deuxième intention a été la metformine + sulfonyles SU (bithérapie).

Les patients ont utilisé l'autosurveillance glycémique dans 96,9% et une éducation thérapeutique a été fournie à 76,9% des patients. Des événements hypoglycémiques majeurs ont été enregistrés chez 1,9% des patients.

Parmi les comorbidités, une hypothyroïdie a été retrouvée chez près de 9% des patients.

Les complications microvasculaires et macrovasculaires n'étaient pas négligeables, mais leur prévalence variait considérablement. L'hypertension était associée chez 38,9% des patients et l'hyperlipidémie chez 20,1% des patients.

Mots clés : diabète de type 2, prise en charge, Algérie

ABSTRACT

The management of patients with type 2 diabetes remains complex and the data of real life remain scarce.

Aims: To describe the baseline characteristics and treatment of patients in Algeria with type 2 diabetes mellitus initiating a second-line glucose-lowering therapy in the global DISCOVER study program.

METHODS

The ongoing DISCOVER program of observational studies DISCOVER (NCT02322762) and J-DISCOVER in Japan (NCT02226822) enrolled more than 15 000 patients in 38 countries including Algeria across six continents. The data collection concerns baseline (initiating a second-line anti-diabetic therapy), 6 months and each year for a follow-up period of three years. The main characteristics recorded are the health parameters and indicators of the management of type 2 diabetes.

RESULTS

293 patients from Algeria were included. Specialties of Main Investigators are Internal Medicine (50%), endocrine-diabetologists (28.6%) and General Practitioner (GP) / Family Doctor (21.4%). Mean age was 55.3 ± 10.7 years with sex ratio M/F of 0.95. The average duration of diabetes was 5.85 ± 4.78 years. Mean Body Mass Index (BMI) was 29.1 ± 4.6 kg/m² and mean HbA1c was $8.3 \pm 1.6\%$. Metformin was the first line therapy in 77.5% of patients and the reasons for changes in treatment were dominated by the lack of efficacy. Dictated by the availability of the drug classes, the first-line treatment was dominated by Metformin, and the second line therapy was Metformin+Sulphonylureas SUs (Dual).

Patients used the Self-monitoring of blood glucose (SMBG) in 96.9% and therapeutic education was provided in 76.9% of patients. Major hypoglycemic events were recorded in 1.9% of patients.

Among the comorbidities hypothyroidism was found in almost 9% of patients.

The microvascular and macrovascular complications were not negligible, but their prevalence varied markedly. Hypertension was associated in 38.9% and hyperlipidemia in 20.1% of patients.

Key words: Type 2 diabetes, management, Algeria

1. INTRODUCTION

Diabetes is an important public health problem and is one of the major noncommunicable diseases^[1]. A steady increase in the number of cases of diabetes and the prevalence of the disease has been recorded in recent decades^[2]. According to the International Diabetes Federation (IDF) in its 8th Edition Atlas, diabetes now affects more than 425 million people, including one third older than 65 years. If nothing is done, the number of people with diabetes could rise to 629 million in 2045^[3].

The problem of type 2 diabetes lies in the close link with cardiovascular diseases^[4]. According to the American Heart Association (AHA) Adults with type 2 diabetes (T2D) have a 2-to-4-fold higher risk for cardiovascular morbidity and mortality than adults without diabetes. Furthermore, the AHA deems diabetes to be "1 of the 7 major controllable risk factors for cardiovascular disease (CVD). Indeed, Adults with diabetes have higher rates of coronary heart disease (CHD), stroke, and heart failure (HF) than nondiabetic adults: – CHD death rates are 2 to 4 times higher – Risk of stroke is 2 to 4 times higher – HF occurs twice as frequently in men and 5 times more frequently in women aged 45 to 74 year^[5].

Algeria is not spared by the global diabetes epidemic^[6]. Diabetes with its complications represents a real public health issue with socio-economic benefits and a very high cost^[7].

Diabetes mellitus remains a major public health problem and Algeria shares with the rest of the world a galloping and disturbing prevalence; In fact, the 2003 WHO STEPwise survey found an overall diabetes prevalence of 8.9% among the 25-64-year-olds^[8] whereas in the 2016-2017 WHO STEPwise among the 19-69 year-olds the prevalence was 14.4%^[9].

The management of patients with type 2 diabetes remains complex and the data of real life remain scarce. The ongoing DISCOVER program of observational studies enrolled more than 15 000 patients in 38 countries across six continents. Algeria was one of the participating countries with 293 patients. The data collection concerns baseline (initiating a second-line anti-diabetic therapy), 6 months and each year for a follow-up period of three years.

The main characteristics recorded are the health parameters and indicators of the management of type 2 diabetes including; site characteristics, physician speciality, patient demographics, the classes of drugs or their combinations prescribed, vital signs and laboratory test results, medical history of type 2 diabetes, including presence of risk factors, comorbidities and co-medications, change(s) in type 2 diabetes treatments during follow-up and reason(s) for change(s), number of major hypoglycaemic events and occurrence of minor hypoglycaemic events, microvascular complications (nephropathy, retinopathy, neuropathy and amputation) and macrovascular complications^[10].

The primary objective of the DISCOVER study program is to describe the disease management patterns and clinical evolution in patients with type 2 diabetes who are starting a second-line glucose-lowering therapy (defined as adding a glucose-lowering drug or switching between therapies) after failure of first-line oral treatment with a monotherapy, dual therapy, or triple therapy.

In addition, the study aims to describe the patient, physician, and healthcare system determinants of treatment patterns, and the associations

between treatment patterns and a broad range of outcomes, including glycemic control, hypoglycemic episodes, incidence of complications (e.g. microvascular and macrovascular events), healthcare resource utilization (e.g. hospitalizations and emergency department visits), and patient-reported outcomes (PROs).

The aim of the present analysis was to describe the baseline characteristics and treatment of patients enrolled in Algeria.

2. MATERIALS AND METHODS.

The DISCOVER Study Algeria is an observational study in real life with the same protocol of the DISCOVER observational study program :DISCOVER in 37 countries (NCT02322762) and J-DISCOVER in Japan (NCT02226822). It included 293 patients spread over 14 sites nationwide. This is a non-interventional study; registered participants undergo clinical evaluations and receive standard medical care as determined by their attending physicians. Patients don't receive any experimental treatment or experimental intervention because of their participation in the study. Participation was voluntary, and patients are free to withdraw from the study at any time and without prejudice to their subsequent treatment.

Data collection is done using an electronic form (eCRF) via a web-based data capture system. For all eligible patients who signed the informed consent form, in addition to the demographic, clinical characteristics are collected at the outset (date of initiating of second-line therapy in add-on or switching after a first-line oral treatment with a monotherapy, dual therapy, or triple therapy) and 6, 12, 24 and 36 months in a 4-month period ($\pm$ 2 months) for a follow-up of three years.

The sites and investigators selected were involved in the management of patients with type 2 diabetes and of different types of physicians (primary care physicians, diabetologists, endocrinologists, Internal medicine, and other specialists) and practices (primary care centers, specialized diabetes centers, and different types of hospitals)

Baseline data will be collected at the routine visit, during which the second-line glucose-lowering therapy will be prescribed. The variables recorded were physiological parameters, laboratory test results, change(s) in glucose-lowering therapy and reason(s) for change(s) (e.g. suboptimal glycemic control and adverse events), HbA1c level at time of change(s), occurrence of microvascular and macrovascular events, occurrence of minor and major hypoglycemic events, changes in comorbidities and co-medications, and healthcare resource utilization.

Statistical analysis

Categorical data are presented as numbers and percentages. Mean (standard deviation [SD]) values, median (interquartile range [IQR]) values are reported, when appropriate.

Descriptive statistics were used to summarize demographic variables, patient characteristics, treatment patterns, lab test results, incidence of complications and hypoglycemic events. Data were stratified by pharmacological drug class and/or individual agent when clinically relevant.

All statistical analyses were performed using the SAS statistical software system (SAS Institute, Inc., Cary, NC).

Ethical and regulatory considerations

This study was conducted under the Guidelines for Good Pharmacovigilance Practices (GVPs) and Good Pharmacoepidemiology Practices (GPPs) issued by the International Society for Pharmacoepidemiology (ISPE), the Declaration of Helsinki and its amendments, and the Algerian Ministry Of Health guidelines. Prior to the enrolment of any patients in the study, the following documents were provided by the site.

- Copy of the IRB/IEC approval letter for the protocol and informed consent (all written information provided to the patient must be approved by the IRB/IEC).

- Copy of the IRB/IEC-approved informed consent document to be used.
- Copy of the protocol sign-off page signed by the investigator.
- Fully executed site agreement.

The study protocol was approved by the Ministry of health and the clinical research Ethics Committee. All participating patients provided signed informed consent.

3. RESULTS

3.1. SITE CHARACTERISTICS.

Fourteen sites have been selected across the national territory and all are in urban areas (100%). These investigation sites included University/teaching hospital (57.1%), Specialized diabetes centre (21.4%), Primary care centre (7.1%), Other type of center (14.3%) and 78.6% of the centers were Public. 57.1% of the investigation sites have Specialty Care (e.g. psychologist, podiatrist).

Specialties of Main Investigators are Internal Medicine (50%), endocrine-diabetologists (28.6%) and General Practitioner (GP) / Family Doctor (21.4%).

3.2. DEMOGRAPHIC, CLINICAL AND BIOLOGICAL CHARACTERISTICS.

In Algeria, 293 patients were included. Mean age was 55.3 ± 10.7 years with sex ratio M/F of 0.95. The average duration of diabetes was 5.85 ± 4.78 years.

More than 90% of patients have insurance coverage and almost 65 % of patients have at least a secondary education level (table 1).

Mean Body Mass Index (BMI) was 29.1 ± 4.6 kg/m² and mean Waist circumference (cm) of almost 90% of patients was 102.2 ± 12.0 .

Mean systolic blood pressure was 128.9 ± 15.0 mm Hg and mean diastolic blood pressure was 75.9 ± 8.9 mm Hg. Mean HbA1c of almost 97% of patients was $8.3 \pm 1.6\%$ and mean Fasting Glucose (mg/dL) of almost 75% of patients was 174.3 ± 60.3 .

Mean LDLc and mean HDLc (mg/dL) of almost 65% of patients were 103.3 ± 34.5 and 42.8 ± 12.2 respectively. More than 99% of patients declared not live alone (table 2).

3.3. PREVIOUS HISTORY OF MACROVASCULAR AND MICROVASCULAR PATHOLOGIES COMPLICATIONS.

The percentages and types of the different microvascular complications (history of chronic kidney disease, retinopathy, retinal laser photocoagulation, auto-nomic neuropathy, peripheral neuropathy and erectile dysfunction) and macrovascular complications (history of coronary artery disease, heart failure, angina, myocardial infarction, percutaneous coronary intervention, coronary artery bypass grafting, stroke, transient ischaemic attack, carotid artery stent, carotid endarterectomy, peripheral artery disease, diabetic foot, amputation and defibrillator use) are shown in (table 3).

The prevalence of microvascular pathologies was greater than that of macrovascular complications.

Hypertension was associated in 38.9% and hyperlipidaemia in 20.1% of patients.

Among the comorbidities hypothyroidism was found in almost 9% of patients, and major hypoglycemic events were recorded in 1.9% of patients (table 4).

3.4. DIABETES TREATMENT: FIRST LINE THERAPY

Among the new antidiabetic classes, only dipeptidyl peptidase-4 (DPP-4) inhibitors (sitagliptin, vildagliptin) and one glucagon-like peptide-1 (GLP-1) receptor agonist (liraglutide) were registered in Algeria, but not reimbursed, which limited their prescription considerably.

FIRST-LINE THERAPY

Monotherapy was the first-line therapy in almost 80% of patients and metformin MET monotherapy was the mostly prescribed first-line

therapy (77.5%), followed by combinations of MET + sulphonylureas SUs (9.9%).

Among first line classes Metformin MET with a mean daily dose of 1866.4 ± 464.6 mg was used in 94.5%, followed by sulphonylureas Sus in 15.3% of patients (table 5, supplementary table).

Change in Anti-diabetic Medication was mostly in an outpatient setting (91% of patients) and the lack of efficacy was the main determinant of moving to second-line therapy (93.2% of patients).

Among the reasons for changing first line therapy we found also; Physician preference (11.6%), Poor adherence (4.8%), Patient Request (4.4%), and Hypoglycaemic Event (2.0%) (supplementary table Change in Anti-diabetic Medication at Baseline).

SECOND-LINE THERAPY:

Combinations of MET + Sus (35.8%) and MET + Meglitinides (22.8%) were the most commonly prescribed second-line therapies whereas Insulin was used in only 8.5% of patients (table 5, supplementary table doses of first and second line).

The choice of second-line treatment was determined by the expected efficacy in 68.6% followed by tolerability 35.8%, convenience 34.8% however the cost was in only 9.6% the reason for choosing the second line therapy.

76.9% of patients received education on diabetes treatment and management in past 1 year and 96.6% used glucose monitoring (supplementary table Change in Anti-diabetic Medication at Baseline).

3.5. CONCOMITANT MEDICATION

43.3% of patients received antihypertensive drugs among which Renine Angiotensin System (RAS) Blockers represented almost 90%, Calcium Channel Antagonists almost (35%), Diuretics almost (28%), and Beta-Blockers almost (20%).

36.9% of patients received Lipid-lowering Drugs among which statin was used in nearly 80% of patients.

30.7% of patients received Aspirin, and 8.2% were treated with Concomitant Thyroid Replacement Drugs.

4. DISCUSSION

In Algeria, this the first observational study in real-world setting that describes the characteristics, treatment and outcomes of patients with type 2 diabetes mellitus after initiating second-line glucose-lowering therapy. Algeria, with 293 patients included, is one of the 38 countries included in the ongoing DISCOVER study (15,992 patients) [10].

As individuals with diabetes require lifelong personal care to reduce the possibility of developing long-term complications. A good knowledge of diabetes risk factors, including obesity, dyslipidaemia, hypertension, family history of DM, and sedentary lifestyle, play an essential role in prevention and treatment. Also, sociodemographic, economic, psychological, and environmental factors are directly and indirectly associated with diabetes control and health outcomes [11].

To provide a comprehensive overview a broad spectrum of investigators' specialities was involved mostly Internal Medicine followed by endocrine-diabetologists and then General Practitioner (GP) / Family Doctor.

The mean age was 55.3 ± 10.7 years with an Africa Region Countries (Algeria and South Africa) overall mean age of 54.9 years younger than Europe Region Countries (Austria, Czech Republic, Denmark, France, Italy, the Netherlands, Norway, Poland, Russia, Spain, Sweden and Turkey) overall mean age of 61.9 years [11]. And this was reported in the literature data [6, 15, 16].

Most patients were with overweight per the mean BMI of 29.1 ± 4.6 Kg/m².

The mean glycemic level of patients was not to the targets recommended by the international guidelines [13,14]; Mean HbA1c was $8.3 \pm 1.6\%$ almost similar to other regions in DISCOVER Study program outside

Europe^[11] and this is expected in a population of patients who were escalating from first- to second-line therapy due to lack of efficacy as the main reason for changing first-line therapy. The most commonly prescribed First-line treatment was Metformin which was compliant with the international guidelines^[13,14]. The most commonly prescribed 2nd line treatment was Metformin + SU and the changes in treatment were mostly determined by efficacy and this was similar in Africa, South-East Asia and the Western Pacific regions however in Americas, Europe and the Eastern Mediterranean regions of the DISCOVER Study program the most prescribed 2nd line treatment was metformin and a DPP-4 inhibitor^[17]. Among comorbidities almost 9% diabetics were treated for hypothyroidism. This is to be taken into consideration given the frequent association, the need for screening and the impact of hypothyroidism in terms of hypoglycemia^[18,19,20,21,22]. Hypertension was documented in 117 patients while 127 patients had been treated with anti-hypertensive drugs mostly with Renin Angiotensin System Blockers (115 patients). Hyperlipidaemia was documented in 59 patients while lipid-lowering drugs were prescribed for 108. 30.7% of patients were taking antiplatelet drugs. According to DISCOVER Algeria data, the rates of microvascular and macrovascular complications standardized for age and sex, were respectively 24.1% and 6.1%. These rates were divergent from other countries with comparable mean HbA1c, example the mean HbA1c of the overall Global DISCOVER Study programme population was $8.3 \pm 1.6\%$ while the prevalence of microvascular complications and macrovascular complications were respectively 18.8% and 12.7% overall^[11]. We assume that the relative low prevalence of macrovascular complications could be explained by a good level of cardiovascular prevention.

5. CONCLUSION:

This observational study summarizes in real world settings the principal characteristics of type 2 diabetic patients. In a sample of 293 patients initiating a second-line anti-diabetic therapy the mean HbA1c in 96.2% of patients was not at the recommended targets. The management of the patients was ensured mostly by specialist doctors. The comorbidities associated with diabetes were hypertension, dyslipidaemia and to a lesser degree hypothyroidism. First-line treatment was consistent with the guidelines but in the second line patients received mainly Sulphonylureas SU and this apparently was due to the unavailability of new drugs. The relative low prevalence of macrovascular complications could be explained by the good level of cardiovascular prevention.

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TABLE 01 DEMOGRAPHIC CHARACTERISTICS OF PATIENTS

		Total
		n = 293
Sex		
(1) Male		143 (48.8%)
(2) Female		150 (51.2%)
Age(continuous)		
Mean ± SD		55.3 ± 10.7
Median (IQR)		53.0 (48.0, 63.0)
Time since DM Diagnosis (Month)		
Mean ± SD		70.2 ± 57.4
Median (IQR)		58.4 (25.8, 97.1)
Living arrangement status		
(1) Lives alone		1 (0.3%)
(2) Does not live alone		286 (99.7%)
Missing		6
Education level		
(1) No formal education		25 (8.9%)
(2) Primary (1-6 years of education)		72 (25.5%)
(3) Secondary (7-13 years of education)		139 (49.3%)
(4) University / Higher Education (13+ years)		46 (16.3%)
Missing		11
Main working status		
(1) Employed		87 (30.3%)
(2) Self-Employed		33 (11.5%)
(4) Not working		112 (39.0%)
(5) Retired		55 (19.2%)
Missing		6
Health insurance coverage		
(1) Private		27 (9.5%)
(2) Public/governmental		241 (84.6%)
(4) No insurance		17 (6.0%)
Missing		8
Tobacco Smoking		
(1) Non-smoker		227 (78.3%)
(2) Ex-smoker		44 (15.2%)
(3) Current smoker		19 (6.6%)
Missing		3
Alcohol drinking		
(1) Lifetime abstainer		275 (94.8%)
(2) Former drinker		14 (4.8%)
(3) Drinker		1 (0.3%)
Missing		3

TABLE2: CLINICAL AND BIOLOGICAL CHARACTERISTICS.

		Total
		n = 293
Weight(kg)		
Mean ± SD		80.0 ± 13.1
Median (IQR)		80.0 (72.0, 88.0)
Height(cm)		
Mean ± SD		165.9 ± 8.9
Median (IQR)		166.0 (160.0, 172.0)
BMI Derived		
Mean ± SD		29.1 ± 4.6
Median (IQR)		28.7 (26.2, 31.6)
Waist circumference(cm)		
Mean ± SD		102.2 ± 12.0
Median (IQR)		102.0 (94.0, 108.0)
Missing Rate		31 (10.6%)

Systolic SBP (mmHg)	
Mean $\pm$ SD	128.9 $\pm$ 15.0
Median (IQR)	130.0 (120.0, 135.0)
Missing Rate	1 (0.3%)
Diastolic DBP (mmHg)	
Mean $\pm$ SD	75.9 $\pm$ 8.9
Median (IQR)	75.0 (70.0, 80.0)
Missing Rate	1 (0.3%)
HbA1C(%)	
Mean $\pm$ SD	8.3 $\pm$ 1.6
Median (IQR)	7.9 (7.3, 9.0)
Missing Rate	11 (3.8%)
HDL(mg/dL)	
Mean $\pm$ SD	42.8 $\pm$ 12.2
Median (IQR)	41.0 (34.5, 49.0)
Missing Rate	97 (33.1%)
LDL(mg/dL)	
Mean $\pm$ SD	103.3 $\pm$ 34.5
Median (IQR)	104.0 (78.0, 122.0)
Missing Rate	104 (35.5%)
Total Cholesterol(mg/dL)	
Mean $\pm$ SD	174.5 $\pm$ 38.8
Median (IQR)	174.0 (152.0, 198.0)
Missing Rate	76 (25.9%)
Triglycerides(mg/dL)	
Mean $\pm$ SD	155.9 $\pm$ 109.9
Median (IQR)	139.0 (99.0, 177.0)
Missing Rate	79 (27.0%)

TABLE 3 : PREVIOUS HISTORY OF MACROVASCULAR AND MICROVASCULAR PATHOLOGIES

	Total n = 293
Any Macrovascular Disease	22 (7.5%)
Coronay Artery Disease	14 (4.8%)
Transient Ischaemic Attack	3 (1.0%)
Peripheral Artery Disease	1 (0.3%)
Diabetic Foot	2 (0.7%)
Any Microvascular Disease	165 (56.3%)
Chronic Kidney Disease	12 (4.1%)
Albuminuria	15 (5.1%)
Retinopathy	13 (4.4%)
Peripheral Neuropathy	29 (9.9%)
Erectile Dysfunction	23 (7.8%)

TABLE 4 :HISTORY OF OTHER PATHOLOGIES

Other pathologies	Total n = 293
Thyroid	27 (9.2%)
Thyroid type	
(1) Hyperthyroidism	3 (11.1%)
(2) Hypothyroidism	24 (88.9%)
N	266
Major Hypoglycaemic events	5 (1.9%)
Missing	26
Minor Hypoglycaemic events	13 (4.7%)
Missing	17

Table 5 : First and second line therapy classes

First Line Class	Total n = 293	Second Line Classes	Total n = 293
(1) Met (Mono)	227 (77.5%)	(1) Met monotherapy	2 (0.7%)
(2) SU (Mono)	11 (3.8%)	(5) AlphGluc (Mono)	1 (0.3%)
(3) DPP4 (Mono)	1 (0.3%)	(7) Met+SU (Dual)	105 (35.8%)
(4) Other (Mono)	2 (0.7%)	(8) Met+DPP4 (Dual)	5 (1.7%)
(5) Met+SU (Dual)	29 (9.9%)	(10) Met+other (Dual)	81 (27.6%)
(7) Met+other (Dual)	18 (6.1%)	(11) SU+Thiaz (Dual)	1 (0.3%)
(8) Other Dualtherapy	1 (0.3%)	(12) Other Dualtherapy	2 (0.7%)
(10) Met+SU+Thiaz (Triple)	4 (1.4%)	(14) Met+SU+Thiaz (Triple)	48 (16.4%)
		(15) Met+SU+AlphGluc (Triple)	11 (3.8%)
		(16) Other Triple Therapy	8 (2.7%)
		(17) 4 or 4+ Therapy	4 (1.4%)
		(18) Insulin (May also receive oral therapy)	25 (8.5%)

SUPPLEMENTARY TABLE : DOSES OF FIRST AND SECOND LINE TREATMENTS.

Doses of first and line treatments	Total n = 293	Doses of second and line treatments	Total n = 293
Metformin	277 (94.5%)	Metformin	283 (96.6%)
Dose	1866.4 ± 464.6	Dose	1838.0 ± 498.0
Missing Rate	0 (0.0%)	Missing Rate	
Acarbose	1 (0.3%)	Acarbose	36 (12.3%)
Dose	50.0 ±	Dose	130.6 ± 271.3
Missing Rate	0 (0.0%)	Missing Rate	0 (0.0%)
Glimepiride	33 (11.3%)	Gliclazide	56 (19.1%)
Dose	4.2 ± 1.6	Dose	47.9 ± 46.3
Missing Rate	0 (0.0%)	Missing Rate	0 (0.0%)
Glyburide/Glibenclamide	5 (1.7%)	Glimepiride	118 (40.3%)
Dose	18.0 ± 6.7	Dose	2.2 ± 1.8
Missing Rate	0 (0.0%)	Missing Rate	0 (0.0%)
Repaglinide	19 (6.5%)	Glyburide/Glibenclamide	4 (1.4%)
Dose	3.7 ± 2.0	Dose	10.0 ± 5.8
Missing Rate	1 (5.3%)	Missing Rate	0 (0.0%)
Sitagliptin	1 (0.3%)	Basal Insulin	20 (6.8%)
Dose	100.0 ±	Dose	11.6 ± 2.5
Missing Rate	0 (0.0%)	Missing Rate	0 (0.0%)
		Basal Bolus Insulin	0 (0.0%)
		Dose	±
		Missing Rate	
		Liraglutide	2 (0.7%)
		Dose	1.2 ± 0.0
		Missing Rate	0 (0.0%)
		Repaglinide	77 (26.3%)
		Dose	2.0 ± 1.6
		Missing Rate	0 (0.0%)
		Sitagliptin	8 (2.7%)
		Dose	100.0 ± 0.0
		Missing Rate	0 (0.0%)

SUPPLEMENTARY TABLE: CHANGE IN ANTI-DIABETIC MEDICATION AT BASELINE

	Total n = 293
Reason for changing First Line Therapy	
Lack of Efficacy	273 (93.2%)
Hypoglycaemic Event	6 (2.0%)
Weight Gain	5 (1.7%)
Side Effect	6 (2.0%)
Patient Request	13 (4.4%)
Poor adherence	14 (4.8%)
Patient convenience	11 (3.8%)
Physician preference	34 (11.6%)
Reason for Choosing a Second Line Therapy	
Efficacy	201 (68.6%)
Tolerability	105 (35.8%)
Weight	17 (5.8%)
Hypoglycemic	30 (10.2%)
Patient request	44 (15.0%)
Convenience	102 (34.8%)
Access Reason	14 (4.8%)
Cost	28 (9.6%)
Other	46 (15.7%)