Non-Interventional Study (NIS) Report Synopsis	
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A NON-Interventional, Multicentre, ProspecTive, ObservAtional Study to UndeRstand Usage and Effect of SaxaGliptin as First Add-On After METformin in Indian Type 2 Diabetes Patients. (ONTARGET-India)

Study dates: 30th October 2015 – 26th December 2016	**First Subject In: 30th October 2015** **Last Subject Last Visit: 26th December 2016**

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NIS REPORT SYNOPSIS (IF APPLICABLE)

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Rationale for this Non-Interventional Study (NIS) Primary

Diabetes is new endemic to India with an estimated 67 million Indian living with this condition in year 2014. Metformin is used as 1st line oral antidiabetic drug in most cases. Sulfonylureas (SU) are used as frequent first add-on after failure of metformin monotherapy. Dipeptidyl peptidase 4 (DPP4) inhibitors are a newer class of incretin based therapy which have a lower incidence of hypoglycemia and are weight neutral. In India, DPP4 inhibitors were introduced in early 2007 but they still remain underutilized mainly because of economic reasons. Also, usage of DPP4 inhibitors is limited in the early stage of diabetes as they are usually preferred as 3rd or 4th add-on therapy.

The existing clinical trial programs on DPP4 inhibitors included limited number of subjects from India. Same is the case with the saxagliptin phase 3 program where only few hundred Indian subjects are studied. There is no study available which evaluates the effect of saxagliptin in real world scenario. Key opinion leaders in diabetes in India have also identified the need for study on Indian subjects to observe the usage pattern and effect of saxagliptin, a DPP4 inhibitor, in the real world setting. Therefore, there is a need for data on real world setting in larger group of subjects across India. With this aim in mind, the present study has been planned.

Objectives

(a) Primary objective: The primary objective of this study is to understand the usage pattern and effect of saxagliptin as first add on after metformin in Indian patients.

(b) Main secondary objectives: The main secondary objectives are to assess effect of saxagliptin on glycated hemoglobin (HbA1c) reduction, reported side effects, hypoglycaemia and changes in quality of life scores.

Study design

This was a multicentre, non-interventional, prospective, observational study and to achieve all objectives of the study, it was planned to screen 1500 patients from 50 centres.

Target subject population

A patient of type 2 diabetes, who were not controlled by metformin monotherapy (minimum dose of 500mg OD for atleast 3 months) and to whom saxagliptin was prescribed within past 15 days.

Study variable(s):

Primary variables: The primary variables of this study included demographic characteristics, disease duration, medical and surgical history including co-morbidities, current medications, HbA1c, saxagliptin discontinuation and reasons for switching over to other medications.

Other Variables: Hypoglycemia, HbA1c reduction, Urinalysis and Changes in WHO Quality of Life-BREF questionnaire (WHOQOL-BREF).

Statistical methods

A sample size of 1500 subjects were sufficient to meet the objectives of the study. The study population were comprised of eligible subjects and Intent to Treat analysis (ITT) was performed.

RESULTS

A total of 1109 T2DM patients were analysed for the study. The mean (SD) age and BMI of all enrolled subjects was 51.17 (11.85) years and 27.13 (4.32) (kg/m^2). Saxagliptin 5 mg was taken by 997 (89.9%) patients and 3 mg by 64 (5.77%) patients. Majority of the patients 971 (99.39%) continued saxagliptin and only 6 (0.61%) discontinued and 967 (98.98%) did not switched over to any other oral anti diabetic treatment and 10 (1.02%) switched over to any other oral anti diabetic treatment. Majority of patients 960 (98.26%) were not on other medications apart from anti diabetic treatment and 17 (1.74%) had other medications apart from anti diabetic treatment. Significant reduction was observed in mean change of HbA1c -0.86 (1.76) from baseline to visit 2 in T2DM patients ($p<0.0001$). No hypoglycemic events were observed in 1080 (97.39%) patients during last month and majority of 939 (96.11%) patients had no hypoglycemic events since last visit. Urinary tract and genital tract infection were observed in 148 (13.35%) and 58 (5.23%) patients. In this study, 1095 (98.7%) patients did not report any AEs and no SAE occurred during the study. All the AEs i.e 15 were of mild intensity.

CONCLUSION

Saxagliptin as add on first after metformin is associated with reduction in HbA1c level and lowers the risk of hypoglycemia in patients with type 2 diabetes mellitus inadequately controlled by metformin alone. Overall, saxagliptin in combination with metformin was generally well-tolerated in this patient population and no new or unexpected safety events were identified.