Once-Daily Saxagliptin Added to Metformin Provides Sustained Glycaemic Control and Is Well Tolerated Over 102 Weeks in Patients With Type 2 Diabetes

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ABSTRACT

- Diabetes is Australia’s fastest growing chronic disease with approximately 600,000 patients currently diagnosed with diabetes. By 2025 it is predicted that 1.5 million Australians will have diabetes. Saxagliptin (SAXA) is a potent selective DPP-4 inhibitor designed for extended inhibition of the DPP-4 enzyme. The long-term efficacy and safety of saxagliptin in patients with T2D and inadequate glycaemic control (HbA1c 7.5%–9.0%) on metformin alone. For the double-blind (DB) short-term (ST) treatment period 740 patients (baseline HbA1c 6.9%) were randomized and treated 1:1:1:1 to SAXA 2.5, 5, 10 mg or placebo (PBO) + metformin (MET) 1800 mg od for 24 weeks. For the open-label extension (LTE) period 705 patients who continued in the LTE based on prespecified glycemic criteria. In summary, in patients with T2D inadequately controlled with MET alone is frequently insufficient to maintain glycemic goals in the face of increasing insulin resistance. Saxagliptin added to MET provided sustained clinically meaningful glycaemic improvements over 102 weeks; control and was generally well tolerated. There were no AdEs with the preferred term of angina or Slavens-Johnson syndrome.

RESULTS (continued)

- Patient disposition for the interim analysis is shown in Figure 1.
- Demographic and baseline characteristics are shown in Table 2.
- Efficacy analyses reflect data prior to rescue.
- Efficacy analyses were also eligible to enter the 42mo LTE; pioglitazone rescue therapy was also available during the LTE based on prespecified glycemic criteria.

METHODS

- Study Design (CV181-014) - 4-arm, parallel-group, international, multicentre trial (Figure 1).
- Population: Patients (age 18-77 yr) with T2D and inadequate glycemic control (HbA1c 7.5%–9.0%) on stable dose of metformin for ≥8 wks prior to initiation of rescue treatment were not included in any treatment group that received saxagliptin added to metformin provided sustained clinically meaningful glycaemic improvements over 102 weeks; and was generally well tolerated with no increase in hypoglycaemia or weight.

INTRODUCTION

- MET is considered standard first-line pharmacotherapy in T2D.
- MET reduces hepatic glucose production and improves insulin sensitivity. However, MET alone is frequently insufficient to maintain glycemic goals in the face of increasing insulin resistance.
- Saxagliptin added to MET provided sustained clinically meaningful glycaemic improvements over 102 weeks; and was generally well tolerated with no increase in hypoglycaemia or weight.

STUDY LIMITATIONS

- There was a decreasing trend in the mean absolute glycaemic targets observed at baseline to week 102 in all treatment groups including PBO with the maximal reduction seen in the SAXA 10 mg group.
- There were no clinically meaningful drug effects on any laboratory safety parameter.
- There was a decrease in the mean absolute glycaemic targets observed at baseline to week 102 in all treatment groups including PBO with the maximal reduction seen in the SAXA 10 mg group.
- There were no progressive declines in mean absolute glycaemic targets observed at baseline to week 102 in all treatment groups including PBO with the maximal reduction seen in the SAXA 10 mg group.
- There were no clinically meaningful drug effects on any laboratory safety parameter.
- Completeness of data for laboratory safety parameters was not open to any missing value imputation; patients were included in the laboratory safety analyses based on the last treatment observation carried forward.

CONCLUSIONS

- Once daily saxagliptin added to metformin provides sustained glycemic control and is well tolerated over 102 weeks in patients with type 2 diabetes.