Oral Semaglutide as Add-on to Insulin in T2D: PIONEER 8

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Purpose

- To add a glucagon-like peptide 1 receptor agonist (GLP-1 Ra) to insulin! to assess the effect of oral semaglutide plus insulin on the rate of hypoglycemia! Treatment guidelines recommend its use as a! effective option in patients with insulin monotherapy.

- Oral semaglutide is one of the first GLP-1 Ras in oral formulation currently in development for the treatment of type 2 diabetes (T2D).

- PIONEER 8 assessed the efficacy, safety, and tolerability of oral semaglutide in combination with three insulin regimens.

Methods

- The PIONEER 8 study was a randomized, double-blind, placebo-controlled, parallel-group phase 3 trial in patients with T2D uncontrolled on insulin therapy.

- Patients were randomized to receive once-daily oral semaglutide, 7, 15, or 30 mg, plus insulin detemir 10 units daily for 52 weeks.

- Randomization was stratified by patient’s current oral hypoglycemic agent (glucovance, sulfonylureas, insulin, or insulin analogs) and by randomized center, respectively.

- A 28% reduction in daily insulin dose was reported in the oral semaglutide 30 mg group vs placebo group (P < 0.001).

- Baseline characteristics were similar across treatment groups (Table 1).

- More patients achieved HbA1c <7.0% and the composite outcome with oral semaglutide vs placebo at weeks 26 and 52 (P < 0.001).

- Nausea was most frequently reported with oral semaglutide (Table 3), and treatment decisions were not affected by nausea.

Results

- The primary endpoint was change in HbA1c, and the primary secondary endpoint was change in body weight (kg), both from baseline to 52 weeks.

- Two scientific questions were addressed by two estimands (Figure 2).

- Of the 721 randomized patients (Figure 4), 95.3% completed the trial.

- At screening, 41.8% of patients were on basal insulin, 38.8% were on oral hypoglycemics, 8.4% were naive, and 11.1% were on other agents.

- Baseline characteristics were similar across treatment groups (Table 1).

- Mean change from baseline to week 52 is shown in Figure 3.

- More patients achieved HbA1c <7.0% and the composite outcome with oral semaglutide vs placebo at weeks 26 and 52 (P < 0.001).

- Nausea was most frequently reported with oral semaglutide (Table 3), and treatment decisions were not affected by nausea.

Discussion

- Patients assigned to oral semaglutide and body weight reductions in week 26 were superior with oral semaglutide than when added to insulin.

- Oral semaglutide may reduce the risk of hypoglycemia associated with insulin use, and may have an insulin-sparing effect at T2D.

- The two consecutive insulin add-on periods allowed both the glucagon-like peptide 1 (GLP-1)-raising effect of oral semaglutide to be observed in a controlled setting, and data to be obtained longer term in a setting more reflective of clinical practice.

Conclusion

- Oral semaglutide can effectively improve glycemic control and replace body weight-increasing oral hypoglycemic agents in patients with T2D on insulin.

- The safety profile was consistent with other GLP-1 Ras.

References