TO002

REDUCTION IN THE RATE OF EGFR DECLINE WITH SEMAGLUTIDE VS PLACEBO: A POST HOC POOLED ANALYSIS OF SUSTAIN 6 AND PIONEER 6

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Background and Aims:

The SUSTAIN 6 cardiovascular outcomes trial (CVOT) indicated that once-weekly (OW) subcutaneous (s.c.) semaglutide may have beneficial effects on kidney function. SUSTAIN 6 and the more recent PIONEER 6 CVOT (oral semaglutide) had similar designs and subject populations; both evaluated the effects of semaglutide compared with placebo on important macro- and microvascular outcomes. This *post hoc* analysis of pooled data from the two trials evaluated the effects of semaglutide vs placebo on kidney function, assessed by estimated glomerular filtration rate (eGFR) slope.

Method:

Data for 6,480 subjects from SUSTAIN 6 (OW s.c. semaglutide 0.5 and 1.0 mg or placebo, n=3,297; median follow-up 2.1 years) and PIONEER 6 (oral semaglutide once-daily 14 mg or placebo, n=3,183; median follow-up 1.3 years) were pooled into two groups: semaglutide and placebo. Annual change in eGFR was compared between semaglutide and placebo in patients with eGFR data at baseline, both overall and by baseline eGFR subgroup (≥30–<60 or ≥60 mL/min/1.73 m^2). Data were analysed using a linear random regression model with individual intercept and time slope. Estimated treatment difference (ETD) between annual rates of eGFR slope (from baseline to timepoint of interest) was calculated at Year 1 and Year 2 (Year 2 data predominantly from SUSTAIN 6); interaction p-values indicated differences between subgroups.

Results:

In the overall treatment population, the annual rate of eGFR change was 0.60 mL/min/1.73 m^2 (95% confidence interval [CI]: 0.31;0.90; p<0.0001) lower with semaglutide vs placebo in Year 1. In the subgroup with an eGFR ≥60 mL/min/1.73 m^2 at baseline, the ETD for semaglutide vs placebo at Year 1 was 0.48 mL/min/1.73 m^2/year (95% CI: 0.13;0.82). Whereas, at Year 1, the subgroup with eGFR ≥30–<60 mL/min/1.73 m^2 had an ETD of 1.07 mL/min/1.73 m^2/year (95% CI: 0.46;1.68) (Table). Accordingly, a numerically larger difference in ETD was observed in the eGFR ≥30–<60 mL/min/1.73 m^2 vs the eGFR ≥60 mL/min/1.73 m^2 subgroup (not statistically significant; $p_{interaction}$=0.21).

Conclusion:

Semaglutide was associated with a significantly smaller decline in renal function compared with placebo in subjects across stages of impaired kidney function at baseline. Although benefits were observed in the overall population, the findings indicate that the primary benefit may be observed in those with established chronic kidney disease.

Table:

Annual eGFR change with semaglutide or placebo and ETD between semaglutide and placebo in pooled SUSTAIN 6 and PIONEER 6 trials

	Semaglutide	Placebo
Overall number of subjects contributing to analysis	3,232	3,231
Annual eGFR change [95% CI], mL/min/1.73 m^2/year	−0.95 [−1.16;−0.74]	−1.55 [−1.77;−1.34]
ETD [95% CI], mL/min/1.73 m^2	Yr 1: 0.60 [0.31;0.90] Yr 2: 1.21 [0.62;1.80]***	
Baseline eGFR subgroups		
≥60 mL/min/1.73 m^2, n	2,375	2,374
Mean baseline eGFR, mL/min/1.73 m^2	85.5	85.8
Annual eGFR change [95% CI], mL/min/1.73 m^2/year	−1.15 [−1.40;−0.91]	−1.63 [−1.87;−1.38]
ETD [95% CI], mL/min/1.73 m^2	Yr 1: 0.48 [0.13;0.82] Yr 2: 0.95 [0.27;1.64]*	
≥30–<60 mL/min/1.73 m^2, n	779	777
Mean baseline eGFR, mL/min/1.73 m^2	47.4	46.9
Annual eGFR change [95% CI], mL/min/1.73 m^2/year	−0.29 [−0.73;0.14]	−1.36 [−1.80;−0.92]
ETD [95% CI], mL/min/1.73 m^2	Yr 1: 1.07 [0.46;1.68] Yr 2: 2.14 [0.92;3.36]**	
p-value for treatment by subgroup interaction (Year 2)	0.21	

*p<0.01;

**p<0.001;

***p<0.0001. eGFR was calculated using the CKD-EPI equation. Data were analysed using a linear random effects regression model with individual intercept and time slope and for subgroups interaction between time slope and subgroups. ETD calculated for semaglutide–placebo. Statistical significance of ETD tested at Year 2. CI, confidence interval; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; eGFR, estimated glomerular filtration rate; ETD, estimated treatment difference; n, number of subjects contributing to the analysis; Yr, year.