MO051

## EFFECTS OF SEMAGLUTIDE ON CHRONIC KIDNEY DISEASE OUTCOMES: A POST HOC POOLED ANALYSIS FROM THE SUSTAIN 6 AND PIONEER 6 TRIALS

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**Background and Aims:** The SUSTAIN 6 cardiovascular outcomes trial (CVOT) indicated a renal benefit with subcutaneous (s.c.) once-weekly (OW) semaglutide vs placebo. The PIONEER 6 CVOT reported cardiovascular safety with oral semaglutide in a similar cohort using a similar trial design. In the present *post hoc* study, eGFR data from the SUSTAIN 6 and PIONEER 6 trials were pooled to evaluate the potential benefit of semaglutide (s.c. or oral) vs placebo on chronic kidney disease (CKD) outcomes.

**Method:** Data from 6,480 subjects from SUSTAIN 6 (N=3,297; median follow-up, 2.1 years; mean baseline eGFR, 76 mL/min/1.73 $m^2$) and PIONEER 6 (N=3,183; median follow-up, 1.3 years; mean baseline eGFR, 74 mL/min/1.73 $m^2$) were pooled for semaglutide (0.5 mg s.c. OW, 1.0 mg s.c. OW or 14 mg oral once daily) or placebo. We evaluated time to onset of persistent eGFR reduction (thresholds of ≥30%, ≥40%, ≥50% and ≥57% [57% corresponds to a doubling of serum creatinine]) from baseline in the overall pooled population and by baseline CKD subgroups (≥30–<60 mL/min/1.73 $m^2$, n=1,699; ≥60 mL/min/1.73 $m^2$, n=4,762; data were missing for 19 subjects). Analyses were performed using a Cox proportional-hazards model with treatment group (semaglutide vs placebo) and CKD subgroup as fixed factors and the interaction between both stratified by trial.

**Results:** In the overall population, the hazard ratios (HRs) for time to onset of persistent eGFR reductions with semaglutide vs placebo were <1.0, but did not achieve statistical significance. In subjects with baseline eGFR ≥30–<60 mL/min/1.73 $m^2$, HRs for semaglutide vs placebo were consistently lower compared with the overall population and, in this subgroup, semaglutide significantly reduced the risk of developing a persistent 30% eGFR reduction vs placebo (Figure; p=0.03). Numerically larger effects were seen with increasing eGFR reduction thresholds in this subgroup, with the exception of the 57% eGFR reduction threshold. No statistically different interactions between treatment and CKD subgroup were observed.

**Conclusion:** The findings of this *post hoc* analysis of pooled data from SUSTAIN 6 and PIONEER 6 on clinically relevant outcomes for CKD support a smaller magnitude of eGFR decline with semaglutide vs placebo, despite relatively short follow-up times. The small number of events at both the 50% and 57% thresholds, and the associated broad confidence intervals, limit the interpretability of the results. In line with previous findings, the data suggest a renal benefit of semaglutide vs placebo in subjects with established CKD. The FLOW trial (ClinicalTrials.gov Identifier: NCT03819153), which is dedicated to exploring CKD outcomes with semaglutide treatment, is ongoing to test this hypothesis in patients with CKD at baseline.

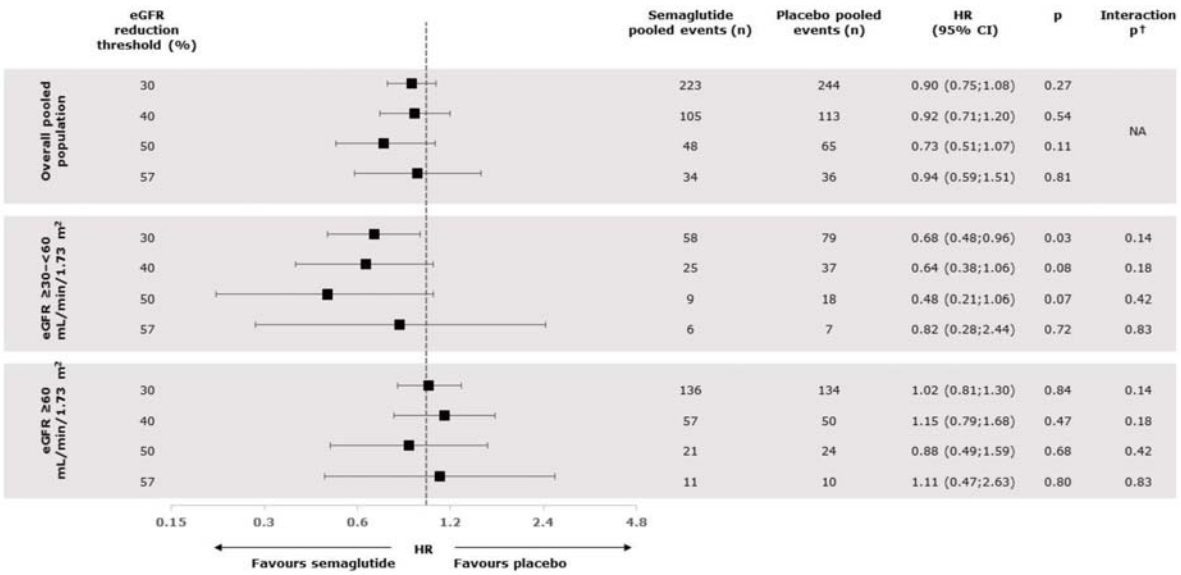


Figure: Semaglutide treatment effect on time to persistent eGFR reduction* across the overall pooled population and chronic kidney disease subgroups: a *post hoc* pooled analysis from the SUSTAIN 6 and PIONEER 6 trials

*Time to 'persistent' reductions in eGFR was defined as the time from randomisation to the first visit in which the value from the subsequent visit was confirmed by fulfilling the same relative reduction from baseline as the value from the previous visit. If no subsequent visit was performed, the confirmation was omitted. †Test for heterogeneity between treatment effects across eGFR subgroups. CI, confidence interval; eGFR, estimated glomerular filtration rate; HR, hazard ratio; NA, not applicable.