Oral presentation 52

Once-weekly semaglutide vs. canagliflozin in type 2 diabetes: results of the SUSTAIN 8 trial

I LINGVAY[1], A CATARIG[2], JP FRIAS[3], H KUMAR[4], NL LAUSVIG[2], CW LE ROUX[5], D THIELKE[2], A VILJOEN[6], RJ MCCRIMMON[7]

[1]UT Southwestern Medical Center, Dallas, TX, USA; [2]Novo Nordisk A/S, Søborg, Denmark; [3]National Research Institute, Los Angeles, CA, USA; [4]Amrita Institute of Medical Sciences, Kochi, India; [5]University College Dublin, Dublin, Ireland; [6]Borthwick Diabetes Research Centre, Lister Hospital, Stevenage, UK; [7]University of Dundee, Dundee, UK

Background and aims: SUSTAIN 8 was a randomised, double-blind, double-dummy phase 3 trial assessing the efficacy and safety of semaglutide, a glucagon-like peptide-1 receptor agonist, vs. canagliflozin, a sodium-glucose cotransporter-2 inhibitor, in subjects with type 2 diabetes (T2D) uncontrolled on metformin.

Materials and methods: Adults with T2D (HbA_{1c} 7.0–10.5%) on stable metformin were randomised to once-weekly subcutaneous semaglutide 1.0 mg or daily oral canagliflozin 300 mg for 52 weeks (N=788). Primary endpoint was change in HbA_{1c}. Secondary endpoints included achievement of prespecified HbA_{1c} targets and change in body weight, and safety assessments. Primary hypothetical estimand was treatment difference (semaglutide vs. canagliflozin) at week 52 for all randomised subjects, if all subjects completed treatment without rescue medication. Primary analysis was an ANCOVA with treatment, stratification, region and baseline as fixed effects. Missing data were handled by multiple imputation using observed data from subjects in the same treatment group.

Results: Baseline characteristics were comparable across treatment groups (**Table**). Semaglutide led to superior reductions in HbA_{1c} from baseline vs. canagliflozin (mean, –1.5% vs. –1.0%; estimated treatment difference [ETD] –0.49; 95% confidence interval [CI]: –0.65;–0.33; p<0.0001). More semaglutide- vs. canagliflozin-treated subjects achieved HbA_{1c} targets of <7.0% (66.1% vs. 45.1%; odds ratio [OR] 2.77 [95% CI: 1.98;3.85]) and ≤6.5% (52.8% vs. 23.6%; OR 4.19 [95% CI: 2.97;5.92]) (p<0.0001 for both). Semaglutide demonstrated superior reductions in body weight vs. canagliflozin (–5.3 vs. –4.2 kg; ETD –1.06 [95% CI: –1.76;-0.36]; p=0.0029). Overall, 22.3% achieved ≥10% weight loss with semaglutide vs. 8.9% for canagliflozin (OR 2.99 [95% CI: 1.89;4.75]; p<0.0001); similar proportions in each group achieved ≥5% weight loss (**Table**). More subjects taking semaglutide vs. canagliflozin achieved composite outcome of HbA_{1c} <7.0%, no weight gain and no severe or blood glucose-confirmed hypoglycaemia (59.9% vs. 39.9%; OR 2.56 [95% CI: 1.84;3.54]), and HbA_{1c} reduction ≥1.0% point and ≥5% weight loss (39.2% vs. 24.3%; OR 1.99 [95% CI: 1.43;2.76]) (p<0.001 for both). Gastrointestinal adverse events (AEs) were the most common AEs with semaglutide (46.9%, n=184); infections and infestations were the most common with canagliflozin (34.5%, n=136). Overall, 9.7% and 5.1% discontinued study medication due to AEs in semaglutide vs. canagliflozin, respectively. There were no unexpected safety findings.

Conclusion: Semaglutide 1.0 mg once weekly led to superior reductions in HbA_{1c} and body weight vs. daily canagliflozin 300 mg.

Table. SUSTAIN 8: key baseline characteristics and efficacy results

	Semaglutide 1.0 mg OW (n=394)	Canagliflozin 300 mg OD (n=394)	Analysis [95% CI]
Baseline characteristics			
Age, years (SD)	55.7 (11.1)	57.5 (10.7)	
Diabetes duration, years (SD)	7.5 (5.9)	7.2 (5.4)	
HbA_{1c}			
Baseline % (SD)	8.3 (1.0)	8.2 (1.0)	
Change at week 52, %-point (SD)	–1.5 (1.3)	–1.0 (1.1)	ETD –0.49 [–0.65;–0.33]**
Subjects achieving ADA target HbA_{1c} <7.0%, %	66.1	45.1	OR 2.77 [1.98;3.85]**
Subjects achieving AACE target HbA_{1c} <6.5%, %	52.8	23.6	OR 4.19 [2.97;5.92]**
Body weight, kg			
Baseline (SD)	90.6 (22.6)	89.8 (22.6)	
Change at week 52 (SD)	–5.3 (5.5)	–4.2 (3.9)	ETD –1.06 [–1.76;–0.36]*
Subjects achieving weight loss ≥5%	51.1	46.6	OR 1.22 [0.90;1.66]
Subjects achieving weight loss ≥10%	22.3	8.9	OR 2.99 [1.89;4.75]**

*p=0.0029 vs canagliflozin. **p<0.0001 vs canagliflozin. Data are observed or imputed from the on-treatment-without-rescue-medication observation period. ADA, American Diabetes Association; AACE, American Association of Clinical Endocrinologists; CI, confidence interval; ETD, estimated treatment difference; OD, once daily; OR, odds ratio; OW, once weekly; SD, standard deviation.

Clinical Trial Registration Number: NCT03136484